ATTENTIONAL RETRAINING ADMINISTERED TO CIGARETTE SMOKERS IN THE FIELD: EFFECTS ON ATTENTIONAL BIAS, CRAVING, AND SMOKING

by

William F. Kerst, M.S.

Dissertation submitted to the Faculty of the
Medical and Clinical Psychology Graduate Program
Uniformed Services University of the Health Sciences
In partial fulfillment of the requirements for the degree of
Doctor of Philosophy 2013

UNIFORMED SERVICES UNIVERSITY, SCHOOL OF MEDICINE GRADUATE PROGRAMS
Graduate Education Office (A 1045), 4301 Jones Bridge Road, Bethesda, MD 20814

DISSERTATION APPROVAL FOR THE DOCTORAL DISSERTATION IN THE MEDICAL AND CLINICAL PSYCHOLOGY DEPARTMENT

Title of Dissertation: "Attentional Retraining Administered in the Field: Effects on Attentional Bias, Craving, and Smoking"

Name of Candidate: William Kerst
Doctor of Philosophy Degree
August 30, 2013

DISSERTATION AND ABSTRACT APPROVED:

DATE: 8-30-13

Dr. David Krantz
DEPARTMENT OF MEDICAL AND CLINICAL PSYCHOLOGY
Committee Chairperson

8-30-13

Dr. Andrew Waters
DEPARTMENT OF MEDICAL AND CLINICAL PSYCHOLOGY
Dissertation Advisor

8/30/13

Dr.Mark Ettenhofer
DEPARTMENT OF PREVENTIVE MEDICINE AND BIOMETRICS
Committee Member

8/30/13

Dr. Cara Olsen
DEPARTMENT OF PREVENTIVE MEDICINE AND BIOMETRICS
Committee Member

COPYRIGHT STATEMENT

The author hereby certifies that the use of any copyrighted material in the dissertation manuscript entitled: "Attentional Retraining Administered to Cigarette Smokers in the Field: Effects on Attentional Bias, Craving, and Smoking" is appropriately acknowledged and, beyond brief excerpts, is with the permission of the copyright owner.

William F. Kerst

[September 6th, 2013]

ACKNOWLEDGMENTS

This dissertation would not have occurred without the support and encouragement of two professors during my undergraduate education. Dr. Xavier Apodaca and Dr. Laurie Dodge went out of their way to ensure that I pursued graduate school. During my graduate education Dr. Andrew Waters took a chance on me before he even formally arrived at the University. His mentorship and intellectual acumen made this a truly thoughtful and enlightening experience. I would like to thank my dissertation committee including Dr. Mark Ettenhofer, Dr. Cara Olsen, and especially, Dr. David Krantz for agreeing to chair the committee despite his numerous other duties. Their insights and contributions helped take this from an outline of a pilot study to a larger scale and ambitious final project.

During data collection and analysis Brigid Rowell, Marilyn Ritzau, Elizabeth Miller, Jessica Forde, Aimee Ruscio, and Cendrine Robinson spent numerous hours running participants, coding data, and providing invaluable advice and support. Dr. Paul Rapp and Dr. David Keyser went to every presentation and listened to every frustration providing valuable moral support and feedback on research design and theory. Finally, thanks to Nicole Kang and Cendrine Robinson for proofreading the final draft of the dissertation and providing useful edits and ideas.

DEDICATION

To Natasha for believing in me.

ABSTRACT

Attentional Retraining Administered to Cigarette Smokers in the Field: Effects on Attentional Bias, Craving, and Smoking:

William F. Kerst, M.S., 2013

Dissertation directed by: Andrew J. Waters, Ph.D., Associate Professor, Medical and Clinical Psychology

Attentional retraining (AR) for cigarette smokers involves training smokers to attend away from smoking cues. According to theory, AR should reduce cue-provoked craving and reduce smoking behavior. Ordinarily AR has been delivered in a laboratory setting. In this study we tested the efficacy of delivering AR on a hand-held computer (PDA) in the field. Cigarette smokers in the Washington D.C. metropolitan area (n=60) were randomly assigned to an AR training group or a control (no training) group. They carried a PDA around for one week and were prompted by the PDA to complete AR (AR group) or a control task (control group) three times a day. They also completed an assessment of attentional bias once per day on the PDA in the field. During the week, AR group participants completed an average of 15.0 attentional retrainings and the control group completed an average of 14.9 control trainings. As hypothesized, attentional bias assessed in the field declined over the week in the AR group, but not in the control group. In a novel eye tracking measure of attentional bias administered post-training, the AR

group spent less time gazing at smoking stimuli compared to control participants. Participants in the AR group reported decreased craving following a smoking cue in field assessments compared to the control group. There was no effect of AR on smoking behavior. The study demonstrated that AR can be administered on a mobile device in the natural environment, and AR can reduce attentional bias and craving.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

LIST OF FREQUENTLY USED ABBREVIATIONS AND DEFINITIONS

Attentional bias: the tendency for smokers to automatically attend to smoking cues and to maintain attention on those cues

Attentional retraining (AR): attention training task designed to alter attentional bias through modified version of tasks (e.g., visual probe) designed to assess attentional bias

Cognitive Bias Modification (CBM): constellation of experimental strategies intended to alter observed cognitive biases in psychopathology

Cue-provoked craving: desire for drugs or other motivationally salient stimuli elicited after presentation of drug related stimuli

Ecological Momentary Assessment (EMA): assessment technique meant to capture participants' status in their natural environment outside the laboratory

Modified VP: Attentional retraining task modeled on the standard visual probe task

Personal Digital Assistant (PDA): small hand-held computer

Questionnaire for Smoking Urges (QSU): self-report questionnaire used to assess craving for cigarettes

Random Assessment (RA): randomly scheduled assessment or retraining task administered via PDA to participants in the field

Reaction Time (RT): observed motoric response time to a given cue (i.e., presentation of dot during visual probe task); usually reported in milliseconds (ms)

Standard VP task: task used for assessment of attentional bias

Visual Probe (VP) task: computerized task involving the simultaneous brief presentation of one valenced and one non-valenced stimulus; one of which is replaced by a target dot to which the participant must quickly respond; intended to assess attentional bias

CHAPTER 1: Introduction

Smoking Cessation

Most smokers report that they are motivated to quit smoking (9). However, most quit attempts are unsuccessful (10, 41, 50). As has been stated previously (47), pharmacotherapies such as nicotine replacement, bupropion, and varenicline improve cessation outcomes (e.g., 45, 94). However, even with widespread availability of resources to support quit attempts (e.g., telephone quit-lines, psychotherapy, and pharmacotherapy), most quit attempts are unsuccessful (9). Much recent research has therefore tried to understand the psychological processes underlying relapse to smoking, in the hope that more effective interventions can be developed.

Automatic and Controlled Psychological Processes

A variety of possible psychological processes contribute to relapse and significant effort has been dedicated to elucidating these processes. There have been important advances in our understanding of these processes but many questions remain. Smokers have described, and researchers have observed, that when abstaining from cigarette use smokers experience acute discomfort resulting from nicotine withdrawal (e.g., 44). This observation suggests the hypothesis that relapse in smokers serves to alleviate this uncomfortable state (the "withdrawal-relief" hypothesis). As has been previously described (47), empirical studies have in general not provided strong support for the simple withdrawal-relief account (89). Most importantly, the association between severity of withdrawal and cessation outcome has been reported to be either somewhat weak or non-existent (42, 70). Moreover, day-to-day changes in stress and affect do not seem to be associated with relapse risk in the first few weeks of a quit attempt (92).

Finally, many relapses occur when participants report being in a neutral or positive mood (90). The finding that smokers often relapse when in a neutral or positive mood seems to contradict the notion that smokers relapse in order to avoid an unpleasant state.

Over the past decade, there has been growing interest in the cognitive processes underlying addiction and relapse (e.g., 120). Researchers in cognitive psychology have described two domains of cognitive process: controlled (or "explicit") processes, and automatic (or "implicit") processes (e.g., 84). Controlled processes are described as having the following characteristics: they occur serially, slowly, require deliberate effort, and are driven by conscious evaluations of input. Controlled processes may be measured reasonably well by self-report (questionnaire) measures. In contrast, automatic processes have an opposite set of characteristics: they occur in parallel, quickly, function without effort, and may not require conscious evaluations of input. Most researchers agree that automatic processes cannot be comprehensively assessed using questionnaires, but can be assessed using computerized cognitive tasks derived from experimental cognitive psychology (e.g., 112).

Attention and Attentional Bias

Attention, while difficult to define, is often conceptualized as consisting of at least two broad components including a state of arousal and awareness and a selective orient-and-focus system (selective attention; 27). In this manuscript the term attention will be used to refer to the selective attention system unless otherwise noted. The selective attention component can be further split into controlled and automatic processes.

Tiffany (103) was the first of numerous subsequent addiction researchers to highlight the importance of automatic processes in the initiation, development, and

maintenance of drug addiction (79, 98 120). An attentional bias to smoking cues is an example of one of these automatic processes in drug addiction. The attentional bias in drug addiction is defined as the tendency of drug users to attend preferentially towards drug-related cues relative to neutral cues in their environment (19). This effect has been observed using a variety of experimental cognitive tasks and in a variety of substance use disorders including cigarette smoking.

As previously described (e.g., 47, 112) the importance of attentional bias to smoking cues is highlighted in Robinson and Berridge's (79) incentive-sensitization theory of addiction. They argue that mental representations of stimuli consistently paired with pleasure become the targets of a particular process, the "attribution of incentive salience." These "incentive stimuli" (those paired with pleasure) subsequently become attractive and wanted, and "grab attention" (79, p. 261). They argue that incentive salience is typically only assigned to stimuli that are consistently paired with pleasure. This makes sense in that individuals' attention would be easily drawn to stimuli that are associated with pleasurable activities, which are important for survival. However, they argue that drugs circumvent pleasure and cause the attribution of incentive salience to drug-related stimuli even in the absence of pleasure. Most importantly, in some individuals, the effect of the drug (on the attribution of incentive salience) becomes more pronounced over time (i.e., sensitization occurs). This is why the theory is termed "incentive-sensitization." As a result of the sensitization of the incentive stimuli, drug-related cues automatically attract the attention of those individuals and exert a strong influence over behavior even if drugs no longer elicit pleasure. This excessive attentional bias has been considered an important component of dependence (e.g., 27).

Attentional Bias, Craving, and Drug Use and Relapse

Franken (27) built on Robinson and Berridge's conceptualizations and provided a more detailed model of the inter-relationships between attentional bias, craving, and drug use (see **Figure 1** for a reproduction of Franken's proposed model). Franken places attentional bias and craving in a reciprocal feedback loop. He suggests that excessive attentional bias contributes to increases in craving which, in turn, contributes to excessive attentional bias (27). Thus, in this feedback system increases in attentional bias can lead to increases in craving which in turn lead to increases in attentional bias. Research on drug craving and attentional bias has found significant relationships between these two factors in cocaine users (28), heroin users (29), and cigarette smokers (114). Furthermore, a meta-analysis concluded that there is a significant, albeit modest, association between drug craving and attentional bias for drug cues (24).

Franken's model also predicts that there should be an association between attentional bias and relapse, partly mediated by craving. Attentional bias for drug cues has been found to prospectively predict outcome in addictive behavior (e.g., 8, 13, 58, 114). Thus, interventions that reduce attentional bias may improve treatment outcomes in the addictions.

Franken (27), when describing his proposed model (**Figure 1**), notes that attentional bias for drug stimuli may also contribute to an increase in drug-related cognitions. Once individuals are aware of the stimuli in their environment, drug users are presumably more likely to think about drugs. For example, they may retrieve episodic memories of drug-taking episodes. These processes may lead to a depletion of attentional resources, and this depletion may undermine cessation attempts. This portion of Franken's model draws on a dual systems theory of drug addiction advocated by Nora

Volkow and Fowler (105) as well as many others (see 37 for a review). With greater attention paid to drug cues and fewer attentional resources to dedicate to alternatives, the risk of drug use and relapse may increase (27). In this manuscript, however, the focus is primarily on attentional bias, craving and smoking. The assessment of other drug-related cognitions or their impact on executive function was beyond the scope of this study.

Visual Probe Task

Cognitive psychologists have devised a number of tasks to assess attentional bias including the visual probe (VP) task (e.g., 55), the modified Stroop task (e.g., 113), and the attentional blink task (e.g., 106). As will be described in detail later, the VP task was used in the current study.

The VP task has been used to assess the automatic allocation of visual attention. It is a reaction time task, and attentional bias is inferred from the pattern of reaction times on the task. For this reason, the VP tasks and other tasks based on reaction times are sometimes described as "indirect" measures of attention. It has long been known that individuals asked to respond quickly to an on screen "probe" stimulus (e.g., a small dot) will do so faster when it is presented in an attended rather than an unattended region (73). A trial of the VP task begins with a picture pair (or word pair) presented on a computer screen. One picture (or word) of the pair is located on the left of the screen and the other is located on the right. One picture contains motivationally salient material (e.g., a snake) and the other picture is motivationally neutral (e.g., a baseball). The picture pair is briefly presented (typically 500 ms) before disappearing with one picture replaced immediately by a probe (e.g., a small dot). The participant is then required to respond to the probe

(e.g., press one of two response buttons which correspond to the dot's position [left or right] as quickly as possible).

A typical finding is that individuals tend to respond faster to probes replacing motivationally salient stimuli than to probes replacing motivationally neutral stimuli (64). This finding is interpreted as indicating that attention has shifted toward the motivationally salient stimulus (i.e., there is an "attentional bias" to the salient stimulus). That is, the mind is processing the region of space that was occupied by the salient picture, which makes it "easier" to respond to the dot when it appears in that location. In the past 25 years, numerous studies have used the VP task to demonstrate attentional biases in a range of psychopathologies, including anxiety (e.g., 55), eating disorders (e.g., 11), and drug addiction (e.g., 51), including tobacco addiction (e.g., 112).

Eye tracking, Cognition, and Addiction

Eye movements are another useful method of assessing cognitive processes (36). Findlay and Gilchrist (26) review the role of eye tracking methodologies in the study of attention and conclude that comprehensive assessment of attentional process must include some component of eye tracking. Many studies of attentional bias in the addictions have included measures of eye movements (as well as reaction time measures) (reviewed in detail below). While reviewing empirical findings on incentive sensitization, Berridge (5) notes the importance of eye movements in addictive behavior and incentive salience in the following quote:

> When attributed to a stimulus representation, incentive salience transforms the mere sensory shape, smell or sound into an attractive and attention-riveting incentive. Once attributed, the incentive percept becomes difficult to avoid

noticing, the eyes naturally move toward the incentive, it captures the gaze and becomes motivationally attractive, and the rest of the body may well follow to obtain it. (p. 380)

The following review and **Table 1** summarize many of the pertinent studies of addiction using eye movements as an outcome measure.

Rosse et al, (81) reported an early study of eye tracking and craving in heavy and light cocaine users. The authors found that heavier cocaine users' visual paths when viewing the image of a crack pipe more closely resembled the crack pipe than did lighter users. Participants reporting elevated cocaine craving were noted to have decreased "lengths" of recorded visual scan path lengths (an early measure of attentional shifting with shorter path lengths reflecting increased attention shifting and increased processing) which the authors interpret as reflecting increased interest in the stimuli. This early study demonstrated a potentially important relationship between eye movements, drug stimuli, and craving in drug users. However, it was not until later that more advanced eye tracking technology would be brought to the study of addiction and visual attention.

One prolific research group has published a series of empirical studies using eye tracking as one of the primary outcome measures (6, 23, 65, 66). In all of these studies the authors used the visual probe task to assess attention through both reaction times in responding to probes and eye movements to simultaneously presented neutral and smoking stimuli. Mogg et al. (65) found that smokers (but not non-smokers) spent more time looking at smoking stimuli (increased dwell time) than neutral stimuli. The authors also found that dwell times correlated with measures of craving and reaction time measures of attentional bias. Mogg et al. (65) also found smokers (but not non-smokers)

were more likely to attend to the smoking picture first (direction of initial gaze fixation). This was one of only two studies reviewed here that reported a significant finding with initial fixation.

Subsequent studies by this research group found no effects of group or stimuli type on initial fixation (6, 23, 66). In these studies smokers consistently exhibited longer gaze duration at smoking stimuli than neutral stimuli, and these dwell times correlated with craving and reaction time measures of attentional bias. A similar pattern of data was reported by another research group using a static dual image viewing task (smoking image paired with a neutral image or aversive image paired with a neutral image; 49). Field et al. (23) suggest that the eye tracking based dwell time measure may be more sensitive to subtle changes in craving and attention than the VP based reaction time measure. A later study by Shoenmakers et al. (85) used an eye tracking measure of attentional bias for alcohol stimuli in heavy social drinkers before and after administration of a priming drink (30mL) of alcohol or non-alcoholic placebo. These authors found that increased attentional bias to alcohol stimuli was evident in reaction time (VP task), gaze dwell time, and initial gaze fixation as a result of the alcohol prime but not after the placebo prime. The authors make no mention of which outcome was more sensitive to changes in attentional bias as a result of the alcohol prime.

A separate research group performed a series of novel investigations of eye tracking and acquired attentional biases in cigarette smoking. In these studies participants were trained to acquire an attentional bias towards neutral images which were repeatedly paired with a significant smoking-related outcome (gaining cigarettes) versus neutral images presented without pairing to a smoking-related outcome (38, 39). Interestingly,

participants acquired an attentional bias for these neutral stimuli (those which were paired with smoking outcomes). To check that their conditioning was effective the authors required a measure of attentional bias. Hogarth et al. (38) used dwell time and reaction times to identify the smoking paired neutral images versus non-smoking paired neutral images as a measure of attentional bias. The authors found increased dwell time and speeded reaction times for neutral images paired with smoking outcomes relative to neutral images not paired with smoking outcomes. In later work by Hogarth et al. (39) the authors used dwell time and the number of fixations on stimuli as the sole measures of attentional bias. Again, they found increased dwell time on stimuli paired with smoking outcomes in cigarette smokers.

More recent research by Miller and Fillmore (63) assessed attentional bias for alcohol cues with eye-tracking based and reaction time based (VP task) measures of attentional bias. The authors used total time spent within a fixation (defined as gaze held within 0.5° for > 100ms) to derive a dwell time measure. This is consistent with dwell time measures used in earlier research on eye tracking and attentional bias (e.g., 85). The authors found that dwell time correlated highly with attentional bias assessed using reaction times. Importantly, Miller and Fillmore (63) report greater effect sizes for the eye-tracking measure ($d = 0.75$) than the reaction time measure of attentional bias ($d = 0.36$); suggesting eye-tracking is a more robust measure of attentional bias. Furthermore, the authors found a significant and positive relationship between attentional bias for alcohol images indexed by dwell time and self-reported drinking over the prior 3 months as assessed by timeline follow-back. This relationship was positive but not significant when reaction time was used to index attentional bias for alcohol images.

Two recent studies used eye tracking measures exclusively to assess attentional bias in alcohol users (80, 116). Consistent with previous findings, in both studies the authors concluded that dwell time is a robust measure of attentional bias for alcohol. Particularly relevant to the current study, Weafer and Fillmore (116) and the earlier described Hogarth studies (38, 39) found that eye-tracking measures of attentional bias were sensitive to a number of experimental manipulations.

Overall, eye tracking measures have been shown to be reliable and sensitive to attentional biases in the addictions. This conclusion is bolstered by the meta-analytic finding that "direct" measures of attentional bias (eye tracking and EEG measures of attentional processing) correlate better with subjective craving in substance users than do "indirect" measures (e.g., manual reaction time to stimuli; 24). When taken together, the studies reviewed here have repeatedly found that dwell time is a suitable eye tracking measure of attentional bias in addiction and may be more consistent than initial orienting in this research.

ATTENTIONAL RETRAINING (AR) IN PSYCHOPATHOLOGY

Most research in experimental cognitive psychopathology has used tasks such as the VP task to **assess** the cognitive processes that underlie the specific psychopathology under investigation. However, in the past few years there has been increasing interest in developing **interventions** that directly target automatic/implicit processes, such as attentional bias (e.g. 60). The idea is that cognitive experimental tasks (e.g., such as the VP) are modified so that they can actually alter the implicit processes they are designed to assess. This emerging field is called Cognitive Bias Modification.

As previously described (108), in a typical cognitive bias modification study, participants perform the "modified" version of the cognitive experimental task. The investigators then examine whether the intervention has had the desired effect on the cognitive bias by assessing performance on the "standard" version of the cognitive experimental task. The investigators also assess whether the intervention influences self-report and behavioral outcome measures.

AR in Anxiety Research

Research in cognitive bias modification was originally stimulated by the work of MacLeod, Mathews, and colleagues in their studies of the cognitive processes underlying anxiety (e.g., 56, 60). Attentional bias in anxiety is the tendency of negative or threatening stimuli to capture increased attention relative to neutral stimuli in the environment in individuals with higher levels of anxiety. Using a modified VP task, these researchers have trained participants to automatically attend towards, or away from, negative stimuli. This form of cognitive bias modification is termed "attentional retraining" (AR). That is, AR is one subtype of cognitive bias modification.

As previously described in Waters and Leventhal (108), in the AR procedure used by MacLeod et al. (56), the probe always replaced negative words for one group of participants (attend-negative group), and for another group the probe always replaced neutral words (attend-neutral group). Both groups received 576 training trials. Attentional retraining influenced attentional bias to negative stimuli, as assessed by the standard VP task (55). Participants in the attend-negative condition tended to be faster to respond on trials in which the probe replaced negative words. Participants in the attend-neutral condition tended to be faster on trials in which the probe replaced neutral words.

Therefore, the AR did significantly influence attentional bias. This was true for stimuli on which participants had been trained as well as for new material (negative and neutral words that were not included in training trials). In addition, participants assigned to the attend-neutral condition reported significantly less anxiety and depression on a subsequent stressor task (an anagram stress task; see also 34).

In a follow up study, MacLeod and colleagues delivered AR in the form of a modified VP task administered remotely over the internet to participants preparing to undergo a real world stressor (88). Participants were Indonesian young adults preparing to relocate to Australia for school. Half of the participants were placed in an attend-neutral condition (trained to attend away from negative stimuli and toward neutral stimuli). Half were assigned to a control (no attentional training) condition. After 15 days of AR or control training, the students relocated as planned. At that time (after relocation), they reported their levels of state and trait anxiety. Levels of state and trait anxiety were both lower in the attend-neutral group than in the control group. Importantly, and pertinent to the present study, the data suggested that attentional bias toward neutral stimuli and away from negative stimuli progressively increased over the 15-day training period in the attend-neutral group alone. This suggests that more "doses" of AR may have greater effects on attentional bias.

In a novel study of the effects of the drug d-Cycloserine (DCS; partial agonist at NMDA glutamate receptors) on AR, Behar and colleagues (4) administered AR for anxiety to a group of participants reporting elevated levels of anxiety. This medication has previously been used to promote fear extinction in conjunction with exposure therapies in anxiety disorders (67) and improve declarative memory in nonclinical

individuals (68). Behar and colleagues administered DCS or placebo prior to administering AR. Training took place on day one of the study and attentional bias was assessed 24 hours later on day two. Participants completed two stress induction tasks on each of the two days of the experiment. The authors found that the participants in the DCS condition displayed a greater reduction in their attentional bias for threat cues from baseline than did participants in the placebo condition. However, there were no effects of drug condition on other anxiety measures in this study. These findings are consistent with expectations in that attentional bias toward threat was reduced as a result of AR but no subsequent changes in anxiety reactivity were observed. However, it suggests possible cognitive and neural mechanisms involved in anxiety and AR (i.e., hippocampal and amygdalar circuits).

In an effort to elucidate the neural mechanisms involved in AR, Browning and colleagues (7) included functional neuroimaging as an outcome measure in their study of AR in anxiety. The authors used the modified VP task to train participants to attend to threat or to avoid threat using the same AR design as MacLeod et al. (55). The AR task consisted of threatening and neutral words as stimuli. The authors then assessed attentional bias for images of threatening faces showing neutral and threatening expressions. They found that the AR significantly increased attentional bias towards threatening faces in the attend-threat condition. No change in attentional bias towards threatening faces nor towards neutral faces was observed in the avoid-threat condition as a result of AR. Browning et al. (7) then used functional Magnetic Resonance Imaging (fMRI) at post-training to assess localized brain activation during performance on the standard VP task using neutral and fearful faces. The authors found differential effects of

brain activation in the lateral pre-frontal cortex (area broadly implicated in attentional processes) of the brain between groups when processing threatening and neutral stimuli. This was the first study to show that AR can alter underlying neural mechanisms involved in selective attention.

Finally, a recent meta-analysis examined the effect of AR in anxiety. The meta-analysis of ten studies with a total of 467 participants reported a medium effect size (d = 0.61) for the effect of AR on anxiety (33; see also 32).

AR in Addiction Research

As previously discussed, Franken (27) provides a model to understand the role of attentional bias and craving in drug use and relapse. Franken notes that interventions that target attentional bias may improve substance abuse treatment outcomes. Franken (27) cites the AR described in MacLeod et al. (56) as an example of an intervention that targets automatic processes. Building on the success of AR in the anxiety literature (noted above), a number of researchers have applied AR in the addictions.

Table 2 summarizes the pertinent published studies of AR in the addictions. In the first study of AR in the addictions, a modified VP task was used to conduct AR in a group of heavy social drinkers (21). The authors randomly assigned participants to an attend-alcohol condition (probe always replaced alcohol stimuli) or an avoid-alcohol condition (probe always replaced neutral stimuli). After AR, attentional bias to alcohol-related stimuli was assessed on a standard VP task. The attend-alcohol group demonstrated significantly increased attentional bias for alcohol stimuli while the avoid-alcohol group demonstrated significantly reduced attentional bias for alcohol stimuli. Finally, after AR, both groups were presented with an *ad lib* alcohol (beer) consumption

session. Participants in the attend-alcohol group were observed to consume significantly more beer than participants in the avoid-alcohol group.

In a follow-up study, Field et al. (22) replicated the finding that AR could significantly influence attentional bias on the standard VP task in drinkers. However, the effects of AR in this study did not generalize to another measure of attentional bias (alcohol Stroop task). Moreover, there was no effect of AR on self-reported craving or alcohol consumption. Schoenmakers and colleagues (86) also reported that AR could influence attentional bias in a group of heavy drinkers. However, AR did not influence self-reported craving or performance on a task purported to be a behavioral measure of alcohol use.

Fadardi and Cox (18) reported an AR intervention for hazardous and harmful alcohol drinkers (defined by U.K. National Health Service standards). The AR was delivered as part of what the authors called an Alcohol Attention-Control Training Program (AACTP). The AACTP includes a trainer and a trainee. The trainer encourages the trainee to increase the speed of his or her reaction times to neutral stimuli. The AR task used in this study was a modified pictorial Stroop with images of alcohol and neutral stimuli overlayed upon a colored background to which the participants must respond. In sample two of the study, hazardous drinkers underwent one week of the AACTP (two sessions separated by one week). Attentional bias to alcohol cues decreased as a result of training and the heaviest drinkers reported an increase in motivation to change their drinking behavior. In sample three of the study, harmful drinkers underwent four weeks of the AACTP (four weekly sessions). Attentional bias to alcohol cues decreased as a result of training and was maintained at a three month follow-up assessment. Also, a

decrease in alcohol consumption was reported at post-training and maintained at three month follow-up. While conclusions in this study are hampered by lack of a control group, it is an important proof of concept of the possible clinical relevance of AR in substance abuse.

Another AR study used a modified VP task in smokers (2). Attentional bias for smoking cues, assessed on a standard VP task, increased in an attend-smoking condition and decreased in an avoid-smoking condition. Subsequent cue reactivity (craving assessed after handling a lit cigarette) was reduced in the avoid-smoking group; however, this effect was only significant in males. Attwood and colleagues (2) acknowledge that changes in cue provoked craving in males only is difficult to interpret they point out that it remains preliminary evidence of an effect of AR on craving. McHugh and colleagues (61) conducted a similar study of AR in adult cigarette smokers using a modified VP task. These authors found that a single episode of AR designed to reduce participants' attentional bias towards smoking cues not only failed to result in a reduction in attentional bias for smoking cues but also failed to reduce cue provoked craving. However, as can be seen in **Table 2**, this study used the fewest number of AR trials of the studies described here and a comparatively large number of assessment trials which may have served to reduce the effectiveness of the AR trials (i.e., administration of a relatively large number of standard VP trials may act to 'counter' the learning of the aforementioned 'If-then implicit production rule').

The most recent study of attentional retraining by Field's group is a study of AR in a sample of cigarette smokers (20). The investigators used a modified VP task with images of smoking and neutral stimuli to retrain attention in light cigarette smokers (> 1

cigarette per week). Participants were randomly assigned to either an attend-neutral, attend-smoking, or control (no training) group. Attentional bias towards smoking cues, assessed with the VP task, increased as a result of training in the attend-smoking condition on trained stimuli (stimuli used for the retraining portion) only. Attentional bias on trained stimuli decreased in the attend-neutral condition and the control condition over time. However, no changes in attentional bias were noted for novel stimuli (stimuli not used in the training) on the VP task. In addition, training had no effect on attentional bias assessed with the pictorial Stroop. No other significant effects were found. The authors acknowledge that their findings were limited by the inclusion of lighter smokers (though 95% of their sample smoked at least 1 cigarette per day) and may have had insufficient statistical power to detect what may be small attentional bias effect sizes in smokers.

The most recent study of AR in the addictions was a randomized controlled experiment examining the efficacy of AR in combination with cognitive behavioral therapy (CBT) for alcohol dependence (87). In this study, the authors randomly assigned 43 alcohol dependent participants in treatment facilities (33 inpatient and 10 outpatient) to either an AR group (called attention bias modification in this study) or a control group. Both groups received CBT as part of the alcohol treatment program in which they were enrolled. The participants underwent five sessions of AR. Training sessions began with an explanation that the training was to help participants improve control over the automatic shifting of their attentional focus towards alcohol cues. AR was delivered via a modified VP task. The control task was a reaction time task involving speeded sorting of specific stimuli into appropriate categories. The researchers found that participants in the AR group showed an increased ability to disengage from alcohol cues. This effect

generalized to novel cues (i.e., cues on which they had not been trained). There was no significant effect of AR on subjective reports of craving. However, the authors found that those in the AR group were released from treatment an average of 28 days earlier (patients were released when their counselors felt they had made satisfactory progress) and took on average 1.25 months longer to relapse.

To the best of our knowledge, Attwood et al. (2), Field et al. (20), and McHugh et al. (61) are the only published studies that have applied AR in smoking. A limitation of all these studies is that AR occurred in a single training session. Thus, the effect of more intensive AR in the context of smoking is not known. For example, other forms of cognitive retraining, such as executive function retraining, often required multiple sessions over several weeks to be effective (i.e., 48). Similarly, AR may require many sessions in order to be maximally effective. This may be particularly true when attempting to train smokers to attend away from smoking cues, given that their preferred response would be to attend toward smoking cues.

Finally, a recent meta-analysis examined the effect of AR in anxiety and appetitive behaviors including smoking (3). The meta-analysis of 37 studies with a total of 2,135 participants reported large effect size (Hedges $g = 1.06$) for the effect of AR on attentional bias in anxiety and a large effect size (Hedges $g = 1.41$) for the effect of AR on attentional bias in appetitive studies. These findings are consistent with the Hakamata et al. (33) meta-analysis of AR in anxiety.

Cognitive Mechanisms of AR

Applications of cognitive bias modification have been growing over the last decade since MacLeod et al.'s (55) seminal 2002 study of AR in anxiety. Commensurate

with this burgeoning exploration of the utility of AR has been a growing examination of the possible cognitive mechanisms which underpin AR in both anxiety and appetitive behaviors (e.g., 3). The description of the attentional bias in both anxiety (elevated vigilance for threat) and addiction (elevated vigilance for appetitive stimuli) and desired outcome in AR (reduced vigilance for threat/appetitive stimuli) suggest the operation of an implicit system operating "behind the scenes". Mathews and MacLeod (60), and later Hoppitt and colleagues (40), suggest that at the most basic level an "implicit production rule" is being learned wherein AR participants develop an 'if-then' statement such that '**if** both threat and neutral stimuli are present – **then** attend to neutral stimuli.' In appetitive behaviors this implicit rule can be thought to operate in a similar fashion to encourage attention away from appetitive stimuli in the presence of neutral stimuli. Ultimately, automatic processes are thought to underlie the development of the production rule and the subsequent unintentional application of this implicit rule to other (untrained) situations or stimuli (AR generalizability). In this proposed mechanism, both the AR and the later generalized effects of AR are thought to operate nearly entirely without conscious awareness. As such, one would expect AR to result in changes in the initial stages of information processing and operate regardless of participants' awareness of training contingencies.

As described here, this implicit learning process shares some features with "probabilistic learning" as characterized by neuropsychological researchers investigating executive functioning and learning impairments in neurological conditions such as Parkinson's disease and schizophrenia (118). "Probabilistic learning" or "probabilistic category learning" is a form of procedural memory learning which involves the learning

of desired (e.g., accurate) responses based on input and feedback without explicit task instructions (119). For example, participants may be asked to make an accurate prediction of a future event based on seemingly unrelated input (e.g., predict the weather based on one of four stimulus cards). Participants are told if their prediction is correct or incorrect and through trial and error consciously learn which cards most often predict a given weather event (i.e., rain). Since probabilistic learning appears to operate through a "conscious realization" of an unspoken rule it stands in contrast to AR in that, in AR, participants are expected to exhibit changes in attentional bias without the need for conscious awareness of the training contingency.

Absent the need for conscious awareness of training contingencies in AR, it seems likely that the cognitive mechanisms underlying AR more closely resemble implicit learning as described by Reber (78). In implicit learning paradigms individuals develop "intuitive knowledge about the underlying structure of a complex stimulus environment" (78, p. 219) through repeated exposure to the structure of that environment. Implicit learning has been most frequently demonstrated in the unconscious learning of artificial grammatical structures through repeated exposure to nonsense words composed with the artificial grammar after which participants are able to identify "correct" grammatical structures (based on the artificial grammar rules) without being able to consciously identify the underlying grammatical rules (77). In the case of AR, participants may be capitalizing on this implicit learning system to unconsciously identify likely target probe positions (i.e., replacing the neutral stimulus with greater frequency). This implicit learning may then generalize to the natural environment through the aforementioned implicit "if-then production rule" without need for conscious awareness.

While a similar automatic cognitive process, or set of automatic processes, may be implicated in appetitive behaviors, Schoenmakers and colleagues (87) suggest that controlled processes may also play a role in some contexts. They found little support for changes in speeded detection of alcohol stimuli as a result of AR for alcohol dependent participants. Instead they found that the AR group showed accelerated disengagement from alcohol stimuli in the AR group. The authors suggested that AR may involve improved control over attentional disengagement of alcohol cues in the presence of neutral cues. That is, participants during AR may use controlled processes to disengage attention from the alcohol stimuli, and that these processes may generalize to real-world settings. Note that, in the Schoenmakers et al. (87) study, AR participants were informed of the contingencies prior to training (i.e., they were correctly informed that the probe would always replace the neutral stimulus which may not necessarily have occurred without these instructions). This may have stimulated the use of controlled processes. In a review of the implicit cognition and addiction literature, Stacy and Wiers (98) also reported support for reduced attentional disengagement from addictive cues. Similarly, a recent review of cognitive bias modification in addiction found more support for more rapid attentional disengagement of addictive cues rather than changes in initial orienting as a result of AR (120). Overall, it is currently unclear whether AR involves primarily automatic processes, or whether this depends on the context of training.

Few studies have examined brain mechanisms underlying AR. Most importantly, to the best of our knowledge no studies have examined the brain mechanisms underlying the *process* of AR. One study of AR used functional neuroimaging to examine the effect

of AR on responses to emotional stimuli (7), but this study did not examine the brain mechanisms underlying the AR procedure itself.

Summary of AR literature

To summarize, modified VP tasks can be used to influence attentional bias. Studies have reported that AR can modify attentional bias to both threat-related (e.g., 60, 88) and drug-related stimuli (e.g., 21, 22). There is also agreement that eye tracking measures are a useful method of assessing attentional processes (e.g., 99). However, eye tracking outcome measures have not yet been utilized in studies of AR in addiction.

Some studies have reported that AR can influence both self-report and behavioral outcomes. For example, MacLeod and colleagues have reported that participants assigned to an attend-neutral (avoid-negative) condition reported less anxiety when subsequently exposed to a laboratory (56) or real-world stressor (88). Three laboratory studies have applied AR to smoking with mixed results. However, all these studies were single-session studies. Thus, the effect of more intensive AR on smoking is not known.

A recent meta-analysis of the effect of AR in appetitive behaviors found large effect sizes in studies with pre-post attentional bias assessments utilizing neutral versus disorder-specific (e.g., alcoholic drinks, cigarettes) stimuli. Importantly, this meta-analysis found that number of training sessions moderated this effect in appetitive studies with more training sessions and trials resulting in more robust outcomes (3). The authors suggest that "it is clear that future ABM [Attention Bias Modification] studies should include multiple sessions in order to obtain larger and perhaps more reliable effects on attention and subjective experience." (3, p. 737).

Ecological Momentary Assessment (EMA)

Researchers have administered AR in a laboratory setting or over the Internet. Ecological momentary assessment (EMA) may be a useful method for extending the scope of AR and for examining its effects on attentional bias. Waters and Li (109) describe EMA as the assessment of experience and behaviors at the moment they occur (the "momentary" part) in a person's natural environment (the "ecological" part). As previously described (e.g., 110), assessments may be done at random times ("random assessments"; RAs), or when participants experience heightened emotions (e.g., feeling particularly stressed). A combination of these random and event sampling strategies can be used (e.g., 90, 109). In the past two decades, EMA has been an increasingly influential methodology in addiction research, particularly tobacco addiction (e.g., 92, 93).

Waters and Li (109) noted that the development of small, hand-held computers (PDAs) has facilitated the collection of EMA data. These devices can be programmed to prompt the person to enter the data, either randomly within a certain period or on a predetermined schedule. In addition, PDAs have several other advantages over pencil and paper diary measures. Compliance can be closely monitored because the data entries are time-stamped (100). Most pertinent to the current study, reaction time tasks can be administered on a PDA (57, 91, 109, 110).

AR and EMA

In the current context, EMA provides a potentially useful method for both administering AR (e.g., using the modified VP task) and for assessing changes in attentional bias over time (e.g., using the standard VP task). It is important to note that if AR administered via a PDA were shown to be effective, it could potentially be delivered

to participants when they are most in need of this intervention (i.e., when attentional bias is elevated). A recent study has demonstrated that attentional bias for drug cues is increased at moments of user identified drug temptation prior to relapse relative to attentional bias at random assessments (57). At times like these, reducing attentional bias for drug cues may be maximally beneficial though challenging to identify and implement. Thus, PDAs may provide a method by which momentary interventions ("ecological momentary interventions") could be delivered at this crucial time.

Massed versus spaced training.

AR delivered in a protracted training program on a PDA may also be more effective than AR delivered at one or two massed training sessions in a laboratory. Delivering the interventions on a PDA over a prolonged period of time is akin to distributed learning. Distributing practice over longer periods of time has been shown in a meta-analysis to be significantly more effective regardless of whether the task was complex or involved mostly motor or mostly cognitive performance (16). The authors found that distributed training was superior to massed for both skill acquisition (outcome measured on the same day; effect size $d = 0.45$, medium) and skill retention (outcome measured $\geq$24 hours later; effect size $d = 0.51$, medium). These effect sizes were not significantly different. Therefore, research supports distributed practice over massed practice for both skill acquisition and retention regardless of the complexity or motor/cognitive features of the task.

Other forms of cognitive training.

Attentional retraining is only one form of cognitive training. While AR in psychopathology has a relatively short history it is basically a computer-assisted

cognitive retraining program (CACR). This modality of cognitive intervention has a broad history that roughly parallels the advent and widespread introduction of personal computers into everyday life (52). As Lynch (52) points out in a historical review of CACR, one of the primary features of these types of training programs is extended training over several days or weeks in a large number of individual training sessions. Recent research has utilized CACR to remediate attention problems in children and adults with Attention Deficit/Hyperactivity Disorder (ADHD) with some surprising success. These programs, as with other CACR, consist of thousands of training trials spaced over the course of several weeks or months (48). From this point of view, AR as a form of CACR, has been handicapped by its frequent deployment in a single lab session. As such, it is not surprising to find small effects and limited generalizability in most existing AR studies.

Increasing the duration and number of doses of training is an important lesson to be learned from the CACR literature, however, there remain other lessons to learn. It is true that many CACR approaches have had limited success with transfer of training to novel ecologically valid tasks (see 52 for a review). However, much like the AR literature to date, many of the studies reviewed by Lynch (52) involved training programs implemented in a laboratory or clinic setting. However, studies of training programs that were implemented in ecologically valid settings (like realistic 'video game' type programs in participants' homes) and involved training of specific tasks were more effective. For this reason, Lynch (52) concludes his review by calling for more research to be done in the field of CACR and recommending, among other things, that CACR be

as ecologically valid as possible. This recommendation serves as further support for the development and deployment of AR into an ecologically valid paradigm.

CHAPTER 2: Background of the current study

PRELIMINARY STUDY

As part of a pilot study of the current study procedures, we tested the feasibility of delivering AR on a PDA in the field (47). Smokers (N=12) were randomly assigned to an AR group or control (no training) group. They carried around a PDA for one week. They were prompted to complete 4 assessments per day, including 3 AR (AR group) or control tasks (control group). One PDA malfunctioned. Participants completed 196 of 255 (77%) of presented assessments. Participants reported that they were not interrupted on the majority (69.4%) of assessments. The data suggested that AR appeared to reduce AR participants' attentional bias towards smoking cues, assessed on the PDA, particularly later in the week. After day 5, attentional bias in the AR group (-29.4 ms) was 46.4 ms lower (more negative) than in controls (+17.0 ms) (pooled SD = 70.7 ms). This pilot study was the first to show that it is feasible to deliver cognitive training on a PDA in ecologically valid settings. We therefore felt confident in conducting a larger scale study utilizing the procedures outlined in this manuscript.

RATIONALE FOR THE CURRENT STUDY

To summarize, attentional bias for drug related cues is an automatic cognitive process implicated in drug addiction. Attentional bias has been hypothesized to be associated with drug craving and is thought to be involved in the maintenance of drug use and initiation of drug relapse. Interventions such as AR that reduce attentional bias may lead to reductions in craving and drug use. AR has been shown to be a promising approach for the treatment of psychopathology, including addiction. AR may be useful in the treatment of tobacco addiction. Few studies of AR have been conducted in tobacco

addiction, and these studies yielded mixed findings. However, these studies were limited in that AR was conducted 1) in a laboratory setting, and 2) in a single-session. Here we examine the efficacy of administering multiple doses of AR on a PDA in a real-world setting.

Specific Aims and Hypotheses

Specific Aim 1.

The primary aim of the study was to examine whether AR - delivered on a PDA - can reduce attentional bias to smoking-related stimuli in smokers.

Hypothesis 1.1.

The AR group will exhibit a significantly lower (more negative) attentional bias toward smoking-related stimuli at a post-training laboratory assessment, compared to the control group.

Hypothesis 1.2.

The AR group will exhibit a progressively lower (more negative) attentional bias toward smoking-related stimuli over time, when assessed on the PDA for a week. The control group will exhibit a consistent attentional bias toward smoking-related stimuli over time, when assessed on the PDA.

Hypothesis 1.3.

The AR group will exhibit a significantly briefer gaze duration on smoking stimuli, when assessed using mobile eye tracking technology, compared to the control group.

Specific Aim 2.

A secondary aim of the study was to examine whether AR - delivered on a PDA - can reduce self-reported craving in smokers.

Hypothesis 2.1.

The AR group will report significantly lower craving at a post-training laboratory assessment compared to the control group.

Hypothesis 2.2.

The AR group will report progressively lower craving over time, when assessed on the PDA for a week. The control group will report consistent levels of craving over time, when assessed on the PDA.

Specific Aim 3.

A tertiary aim of the study is to examine whether AR - delivered on a PDA - can reduce smoking behavior.

Hypothesis 3.1.

The AR group will exhibit a significantly lower level of cotinine (a metabolite of nicotine) in saliva at post-training compared to the control group.

Hypothesis 3.2.

The AR group will report progressively lower levels of cigarette consumption over time, when assessed by a daily diary for a week. The control group will report consistent levels of cigarette consumption over time, when assessed by a daily diary.

CHAPTER 3: Methods

Please note that the methods reported here have been previously described as part of the preliminary pilot study of these procedures (47). Portions of the methods, as described here, are adapted from Kerst (47).

PARTICIPANTS

Participants were 60 adult community-based smokers in the Washington D.C. metropolitan area recruited via local advertisements for smokers. Non-smokers were not included as our primary interest was in the utility of AR to reduce attentional bias (and craving) to smoking cues; this would not be relevant for non-smokers because they typically do not exhibit attentional bias (or craving) to smoking cues (112). Participant recruitment was accomplished by advertising for smokers age 18 – 65 in a local newspaper, Craigslist.com, and through the use of flyers. Participants were paid $20 for each of two laboratory visits as well as $5 per day that they contributed data to the study up to a maximum of 7 days and $2 for each RA that they completed. To qualify, participants had to be current smokers, smoke 10 or more cigarettes per day for the past two years, and be aged 18 – 65. If they were a federal civilian employee or member of the military they had to have their supervisor's approval for participation. Exclusion criteria included expired breath carbon monoxide levels lower than 10 ppm or any other factor that, in the judgment of the investigators, would likely preclude completion of the protocol. **Figure 2** provides the flow of participants through the study.

PROCEDURES

First Session

Participants first contacted the researchers by leaving a phone message expressing interest in the study and leaving their contact information. Research staff returned participants' phone calls and conducted a telephone screening to ensure participants met criteria for inclusion and were interested in participating. If participants were eligible to participate in the study they were invited to attend an initial orientation session. If the participant was eligible, this visit also served as the first laboratory (baseline) visit. At this first visit, study personnel provided a detailed description of the study, answered questions, confirmed eligibility, and obtained written informed consent (see **Appendix B**). The informed consent and verbal description of the study did not reveal the nature of the retraining or group assignment. Individuals who declined to participate or were ineligible were given self-help materials and a referral to smoking cessation programs (if interested).

Next, participants were asked to provide a breath sample by blowing through a carbon monoxide (CO) monitor. If the CO monitor indicated that a participant's expired CO level was very low (less than 10 parts per million (ppm)), he or she was excluded from the study. This is because, if an individual's expired CO level was below 10 ppm, there was serious doubt as to whether the individual actually smoked at a rate of 10+ cigarettes per day (97).

After signing the consent form, the participants were randomly assigned to the AR or Control condition stratified by gender according to a randomization list. However, due to researcher error 16 males and 14 females were assigned to the control condition. The randomization consisted of three blocks of 10 participants. Within each block, 5

participants were assigned to the AR condition and 5 to the Control condition. Thus, in total, 30 participants (15 males, 15 females) were to be assigned to the AR condition and 30 to the Control condition (16 males, 14 females). The participant and the research assistant were both blinded to condition assignment. Eligible participants then completed the VP task on the PDA in the laboratory to assess baseline attentional bias.

Participants also provided a saliva sample for analysis of cotinine levels. (Cotinine is a metabolite of nicotine – see *Biological Measures* in *Measures* below). Participants then completed a demographic questionnaire, a smoking history questionnaire, the Fagerstrom Test for Nicotine Dependence (FTND; 35), the Balanced Inventory for Desirable Responding (BIDR; 71) and the Questionnaire for Smoking Urges (QSU; 104) using the Questionnaire Development System (QDS) computerized questionnaire delivery system. (Data from the BIDR are not reported in the current report). At the conclusion of the first laboratory session participants were given a smoking diary. They were asked to make an entry each day before they went to bed indicating how many cigarettes they had smoked on that day. Participants were told that they could smoke as much or as little as they like during the week. These diaries were collected from the participants at the second laboratory session.

Participants were trained on the use of the PDA at the end of the first laboratory visit. As has been previously described (109), all EMA procedures were implemented on an HP iPAQ running the Microsoft Windows Pocket PC operating system. Application programming was done in C#.NET by Terminal C, a Houston-based company. The PDA uses a stylus-based, touchscreen system. Participants navigated through the software and entered data by touching the stylus or their finger on the screen. The PDA could be

carried in a shirt pocket or purse. Participants were also offered the use of a carrying case to protect the PDA and to facilitate their carrying the PDA at all times. **Table 3** lists all study procedures and measures.

EMA Procedures

In the EMA portion of the study participants carried the PDA around with them as they went about their daily lives. The PDA was programmed to prompt participants four times daily at random times to complete assessments. Using the selected wake up time and bed time on a given day, the program divided the day into 4 equal "periods". Individual RAs were scheduled at a random time during each period. In the AR and control groups respectively, trainings occurred as follows: earlier than 11.00, 17.5% and 13.1%; 11.00-15.00, 30.3% and 29.5%; 15.00-19.00, 34.7% and 38.5%; later than 19.00, 17.5% and 18.9%.

Three of the RAs were AR tasks (for those in the AR condition) or control tasks (for those in the control condition). One RA per day was a standard VP task (for all participants) to assess daily changes in attentional bias. At each assessment (AR, control, and standard VP task) the participant first completed questions assessing their current mood and craving.

Second Session (Visit 2)

After one week participants returned to the laboratory with their PDA for the second and final laboratory visit. At this session participants again completed the standard VP task on a laboratory PDA. They also completed the QSU once again, provided a breath sample for post-training CO analysis, and a saliva sample for post-training cotinine analysis. Participants then completed the mobile eye tracking portion of

the study. Participants were excluded from analysis if they did not attend the visit 2 session before day 14. This criterion was included to reduce the amount of time between the week long training period and the second laboratory session.

Mobile Eye Tracking Task.

For this study the A-S-L (Applied Science Laboratories) Mobile Eye system was used. This eye tracking system is designed to operate without being tethered to a computer. It consists of a wearable digital video recorder (worn around a participant's hips) which is connected to lightweight spectacle mounted optics. The optics include a spectacle mounted mini-camera and monocle that reflects a cornea image illuminated by infrared LEDs to capture eye gaze relative to a scene video captured by a second spectacle mounted mini camera. The eye camera and the scene camera are both located above the right eye. The resolution of the scene video recorder is 640 X 480 pixels with a 60^0 horizontal field of view. Technical data provided by ASL on the accuracy of the Mobile Eye state that with proper calibration the system is accurate to within 1^0 of a visually targeted point. The eye camera and scene camera are hard wired from the back of the glasses to the lightweight carrying case. The recording device interleaves the eye and scene videos into a single video file. This interleaved video is then transferred to a password protected laptop where it is saved as a digital video for later analysis using GazeTracker software specifically designed for analyzing mobile eye tracking data. The interleaved video images are separated and a scene video created with a variable cursor overlay. The gaze location is recorded at 30 Hz and mapped to the 640 X 480 pixel display scene video. The resulting scene video with cursor overlay allows for viewing the

participant's environment while also viewing the relative gaze location. The A-S-L Mobile Eye has been used in a number of research settings.

A participant was first fitted with adjustable glasses in the laboratory interview room in which they completed the other Visit 2 procedures. The eye tracking system was individually calibrated for each participant. Calibration was conducted by having participants individually fix their gaze for approximately 3 seconds on each of 9 calibration points placed across an approximately 3 foot by 3 foot grid on a wall in the interview room. Participants were calibrated at a distance of approximately 4 feet from the calibration points. This calibration distance minimizes the effect of the parallax error on point of gaze accuracy when entering the experimental room. The scene camera of the mobile eye tracking headset is positioned several inches above the eye. Since the system is calibrated from these two points (the eye and the scene camera) on one calibration distance, tracking accuracy of stimuli viewed from other than that calibrated distance will be reduced. A suggested compromise for this problem is to calibrate the system at a distance half of the distance of the closest and farthest stimuli to be tracked. The distance from the doorway to the smoking stimuli in the experimental room is approximately 8 feet and the chair is positioned directly in front of the desk on which the smoking stimuli are sitting resulting in an estimated distance of smoking stimuli from head mounted eye tracker of approximately 2 feet. Half this distance is 5 feet which corresponds well to the calibrated distance of approximately 4 feet. Technical data provided by ASL on the mobile eye system demonstrated that the parallax error increases markedly at closer than calibrated distances rather than farther than calibrated distances. For the mobile eye system used in this study, calibrated at approximately 4 feet, the accuracy of the tracked

gaze location is maximized within 1° of the actual gaze location if the distance from the eye and the scene plane is between 3 - 12 feet.

After calibration, the researcher led the participant into another room used as a smoking laboratory (28-102). The researcher stated to the participant that he or she (the researcher) needed to complete setting up a task in the cognition lab (28-101). In 28-102 there was an unlit cigarette positioned in an empty ashtray with a lighter next to it. The environment in this new room was the same for all participants. Other items in the room were neutral and included: a computer and monitor on a desk; an empty coffee mug; a small plant; an air purifier on the ground; a desk chair; a telephone; and artwork on the wall. The participant was seated in the chair and left alone in the room for 1 minute. During that time, the participant was free to look around the room at his or her leisure.

At the end of the second laboratory assessment, participants were debriefed on the purpose of the mobile eye assessment. Specifically, the researcher informed them: "As you know from the consent form, the purpose of this behavioral research study is to evaluate a new method of influencing smokers' attention, cravings and smoking. When you wore the spectacles, we wanted to know at what you were looking. If one of the training conditions changes how your attention works, it may influence how long you spent looking at different objects in the smoking room or the order in which you looked at them. By measuring your eye movements we can test if the training conditions influenced this aspect of your attention."

Using the data collected by mobile eye tracking we assessed the time that the participant spent looking at the smoking stimuli and neutral stimuli (any other areas in the smoking lab). If AR causes participants to attend away from smoking stimuli (as

hypothesized), we would expect participants in the AR condition to gaze at the cigarette for a briefer duration than those in the control condition. The mobile eye assessment lasted about 6 minutes in duration (including calibration).

MEASURES

Visual probe task.

The visual probe task, whether assessed in the lab or field, was administered on the PDA. The task always begins with text presented on the screen which informed participants that they would be performing a quick task assessing reaction times; they were asked to find a quiet place. They were instructed that a dot would be presented on the left or right hand side of the PDA screen. They were asked not to use the PDA stylus but to indicate the position of the dot as quickly as possible by pressing a "Left" or "Right" button on a PDA screen using only their thumbs (**Figure 3**).

The standard VP task was based on that used by Waters, et al. (114). It consisted of 80 experimental trials, presented in a new random order at each assessment. At the start of each trial, a fixation cross was displayed in the center of the screen for 500 ms. Immediately after presentation of the central fixation cross, two pictures were presented for 500 ms, one on the left side of the central position and one on the right side. Following offset of these pictures, a dot probe was displayed (see **Figure 3** for an example of the task with times). The trial was not complete and the dot did not offset until the participant pressed either the "right" or "left" button corresponding to the location of the dot relative to the central position. After the participant responded, the fixation cross for the subsequent trial was presented.

As previously stated, in the AR or control tasks there were 160 VP trials presented. In the assessment task (standard VP task) there were 80 VP trials presented. Every smoking image was presented once in four different conditions as a consequence of two within-subjects variables: on screen location of the image (left or right) and dot probe (left or right). Taken together, the dot probes replaced the smoking image and neutral image with equal frequency on all administered trials of the assessment task.

Incorrect responses to probe location were discarded. In an effort to reduce spurious effects of reaction time outliers (see 75), those recorded as less than 100 ms were not included in analysis. We computed an attentional bias score as the difference in median reaction times on trials where smoking pictures were replaced by the probe vs. trials where the neutral pictures were replaced by the probe. Faster reaction times on probes that replace smoking pictures than probes that replace neutral pictures (a positive attentional bias score) reflects an attentional bias towards the smoking picture. Thus, if a participant on an assessment has a median reaction time (correct responses) of 500 ms on probes that replace neutral pictures and a median reaction time of 490 ms on probes that replace smoking pictures, the attentional bias on that assessment is +10 ms (500 - 490). Faster reaction times on the probes that replace neutral pictures than probes that replace smoking pictures (a negative attentional bias score, or, "bias in the opposite direction") reflects an attentional bias away from the smoking pictures (and towards the neutral pictures), or "avoidance." Thus, if a participant on an assessment has a median reaction time (correct responses) of 490 ms on probes that replace neutral pictures and a median reaction time of 500 ms on probes that replace smoking pictures, the attentional bias on

that assessment is -10 ms (490 - 500). An attentional bias score of 0 ms reflects no difference in median reaction times between the two probe conditions over time.

Laboratory self-report measures

Appendix A lists the self-report measures used in this study. Laboratory self-report measures included a demographics questionnaire which asked participants to provide their age, gender, race/ethnicity, income, and other demographic data. The smoking history questionnaire contained questions relating to the participants' smoking behavior currently and in the past. Questions included how many years they had been smoking, and how much they smoke on average, and what kind of cigarettes they smoke (i.e., menthol or regular).

The Fagerstrom Test of Nicotine Dependence (FTND) is a self-report measure of nicotine dependence that yields scores from 0 – 10 with greater values reflecting greater dependence (35).

The Balanced Inventory of Desirable Responding (BIDR) is a self-report measure of socially desirable responding (71). (As noted earlier, data from the BIDR are not presented in the current manuscript).

The Brief Questionnaire for Smoking Urges (QSU-brief) is a self-report measure of craving (14). This 10-item measure incorporates two separate factors, each with its own derived score. Factor 1 assesses anticipated smoking pleasure as well as desire and intent to smoke. Factor 2 assesses nicotine 'withdrawal-relief' (lessened negative affect through reduce and nicotine withdrawal) and feelings of urgent smoking need. The total score (Cronbach's alpha = .95 at baseline and .92 at Visit 2) is reported in the current study.

Biological measures.

Salivary cotinine is considered the "gold standard" for measuring nicotine exposure (69). Salivary cotinine was assessed by asking participants to ensure they had not eaten or drunk anything over the last 30 minutes. If participants had not eaten or drunk anything, they were asked to carefully place a small sterile cotton swab in their mouth to allow for saliva absorption. This cotton swab was then placed in a centrifuge to extract the saliva from the cotton. The saliva sample was then sealed with tamper resistant tape on which only the participant number and visit number was written. The sample was then frozen before being shipped to Salimetrics for the cotinine assay.

Exhaled CO levels were measured with a CO monitor and provide an additional measure of exposure (97). Exhaled carbon monoxide (CO) provides a convenient measure of recent smoke intake. The participant's CO level was obtained at the outset of both laboratory sessions. The CO monitor was calibrated from a cylinder of research gas with a known CO concentration (about 50 ppm) regularly.

PDA self-report assessments

The PDA self-report assessments and procedures described here have been previously described in other studies (e.g., 109, 115). Participants responded to the following items on 7-point Likert-type scales (1 = Strongly Disagree, 7 = Strongly Agree) according to their feelings "right now": 1) Craving - A single item was used to assess craving for cigarettes; 2) Difficulty concentrating - A single item was administered to evaluate difficulty concentrating, used in previous EMA studies (e.g., 91); 3) Affect - Items included: enthusiastic, happy, relaxed, bored, sad, angry. Two additional items assess overall mood and energy/arousal levels; 4) Anxiety - A 6-item version of the STAI

(upset, worried, frightened, calm, secure, self-confident) was administered; this abbreviated version has been used in other studies (83); 5) Hunger - A single item assessed the degree of hunger. In addition, 3 items assessed testing and lighting conditions (e.g., whether they are currently indoors or outdoors); 2 items assessed context (whether participants were alone or with others, and whether they were at home/work/ in transit/at a bar or restaurant/somewhere else); 2 items assessed the degree of alcohol/coffee consumed in the past two hours; 1 item assessed whether participants had smoked so far that day; and 1 item assessed the recency of the last cigarette smoked (Response Options: 1=no cigarettes smoked for > 2 hrs; 2=last cigarette smoked between 30 min and 2 hrs; 3=last cigarette smoked between 30 min and 5 min; 4=Just smoked/smoking now). In the current report, data from negative affect, anxiety, difficulty concentrating, and context are not reported because they are not germane to study hypotheses.

We also included a second craving item which assessed craving in response to a smoking cue. Specifically, on each PDA assessment, a smoking picture with neutral features (see **Figure 4** for an example) was presented for 1 second. Participants subsequently reported their craving on a 1-7 scale. The rationale for including this additional craving item was as follows. If AR causes attention to be drawn to neutral features in the picture (as is hypothesized), then "exposure" to the smoking content should be reduced and therefore there should be less cue-provoked craving.

Order of PDA assessments.

Upon prompting, the participant would interact with the PDA to initiate the assessment. The first assessment was the cue-provoked craving measure. So, upon

initiating an assessment a smoking cue (picture) would be displayed on screen for 1 second (in "landscape" mode) and then the cue-provoked craving question was administered. After the cue-provoked craving measure, the self-report questions were administered. They assessed mood and context. During these questions the second (non-cue-provoked) craving question was presented. Following the self-report items, instructions for completing the VP task were presented. The instructions were immediately followed by the VP task (AR task, Control task, or standard VP assessment).

At the conclusion of the VP task the participant was asked how many times he or she was interrupted during the completion of the VP task (Response options: No times, 1 time, 2 times, 3 times, 4+ times). This item was administered so that data could be analyzed while excluding assessments with a large number of interruptions, which presumably yield less reliable data.

Mobile eye tracking

Data collected during the mobile eye tracking portion of the study were analyzed with GazeTracker software developed by EyeTellect, LLC. This software interfaces with the recorded MobileEye data and video to allow for user created lookzones which are manually mapped to the 640x480 pixel scene video. A lookzone, or area of interest, is defined as a manually drawn user defined area placed over stimuli in a particular area of interest on the scene video. Two independent raters blind to participant group assignment manually mapped a smoking stimuli lookzone over the smoking stimuli in the experimental room when these stimuli were visible on the recorded scene video. Both raters were naïve to this software and received the same training by a researcher trained by ASL staff on use of the MobileEye and GazeTracker software. Raters were informed

to create a lookzone such that all of the smoking stimuli would be within the lookzone but extraneous stimuli would not be incidentally in the lookzone. The defined lookzones were then manually resized and moved around the recorded scene video as participants moved about the room (see **Figure 5** for an example of gaze location and lookzone captured during coding with example outcome data). When smoking stimuli were not on screen the lookzone was moved to a neutral area outside of the recorded scene video so that no gazepoints could be recorded in the lookzone when smoking stimuli were not visible. Raters manually moved and resized the smoking stimuli lookzone while reviewing the video data at 1/10th video speed stopping as required to make manual adjustments to the size and location of the lookzone. Both raters followed these same procedures.

We analyzed data from both the first 5 seconds of the task and the entire 60 seconds. The first 5 seconds were considered important because it would capture whether the smoking stimuli would automatically capture the participant's attention as they entered the room. The 5 second portions of data were captured starting from the moment participants crossed the threshold of the experimental room and ending exactly 5 seconds from that time. The 60 second portions of data were recorded with the exact same starting point as the 5 second clip but persisted for the entire initial 60 seconds of the participants' entry into the room. Eye tracking data and video were trimmed by one researcher and these data were utilized by the blind raters for the aforementioned analysis. Informed by the literature review, total time looking at the smoking stimuli and number of gazepoints recorded within the smoking stimuli lookzone were the two variables of primary interest (e.g., 6, 23, 66).

GazeTracker software default settings were used for this study. These default settings are similar to the settings used by other researchers conducting desktop eye tracking tasks with fixed eye tracking hardware (e.g., 65). For this study the following settings were used: a gazepoint was defined as an individually recorded point of data at each digitization point. There are a possible 30 gazepoints recorded per second. Therefore each gazepoint corresponds to 33.33 ms of tracking time. Total time tracked is calculated from recorded gazepoints. However, there is not a direct correspondence between gazepoints and time tracked for the following reason. If two gazepoints were recorded with no more than one missing gazepoint between them no recorded time was logged as lost. (In contrast, the missed gazepoint is not counted in the total number of gazepoints). These points notwithstanding, number of gazepoints on smoking stimuli and total time on smoking stimuli were highly correlated in this dataset ($r = .97$).

An additional reported eye tracking metric is number of eye gaze fixations. A fixation is broadly defined as an individual eye gaze behavior wherein gaze is maintained in a fixated area long enough to allow visual processing and thus cognitive processing to occur. Gazetracker software settings defined fixations as 3 or more gazepoints recorded within a 40 pixel diameter for >200 ms. Fixation data were recorded and reported in outcome tables reported later. However, there are considerable challenges in accurately recording fixations with mobile eye tracking hardware without also assessing head and body movements independently (17). As a compromise we decided to calculate and report gaze duration in the smoking stimuli lookzone independent of the fixation criteria. However, analyzing overall gaze duration (instead of duration fixated) in the lookzone may be susceptible to eye movements occurring within the lookzone without sufficient

duration to allow for processing (such as very brief and very fast eye movements called saccades). Saccades are most directly captured and identified with fixed desktop eye tracking applications by identifying the velocity of eye gaze shifts from point to point (82). Saccades are fast (>300 visual degrees per second) and fixations are slower (<100 visual degrees per second). However, the recording frame rate of 30 Hz is too slow to capture sufficient data points to accurately calculate the velocity of gaze shifts (17). As such, saccade and fixation identification is challenging and at least partially inaccurate in mobile eye tracking as head and body movements can make gazepoints appear to move around the scene video despite remaining fixed on an actual item in the environment.

In sum, three dependent variables were extracted for analysis: time spent within the smoking stimuli lookzone (gaze duration, in units of seconds); number of recorded gazepoints in smoking lookzone (in units of number of gazepoints, each of 33.3 ms); and number of fixations within the smoking stimuli lookzone. The first two were given more weight as they are without the challenges involved in identifying fixations, and their derivation required fewer assumptions. All these outcomes were computed for the first 5 seconds and the entire 60 second period.

Data from the two raters were highly correlated for these three measures for both the 5 second clip (Pearson's r = .97, .98, and .97 for time spent in smoking lookzone, no. of gazepoints in smoking lookzone, and no. of fixations in smoking lookzone respectively) and the 60 second dataset (Pearson's r = .99, .99, and .98 for time spent in smoking lookzone, no. of gazepoints in smoking lookzone, and no. of fixations in smoking lookzone respectively). We took a mean of the two raters scores as the dependent variable with the exception of one subject in which data from a single rater

were used because data from the other rater were lost due to experimenter error. (Data from this participant were not used in the computation of the inter-rater correlations described above).

Stimulus Materials

Pictures for the VP tasks were taken from the International Smoking Image Series (ISIS; 31), previous published studies (101, 107), and our own original pictures. Pictures were selected from an original pool of more than 300 pictures. The pictures were categorized based on both valence (smoking vs. nonsmoking) and content (human vs. no human). This grouping yielded four categories: smoking-human, nonsmoking-human, no-human-smoking, no-human-nonsmoking. Pictures were then distributed to research staff who rated the overall quality of the image as a salient stimulus based on its category on a 0 (not good) – 5 (very good) scale (e.g., a good human smoking picture). These ratings were then averaged across researchers for each picture and the highest rated 20 pictures from each category were chosen for inclusion in the final set of 80 images. These 80 pictures (20 smoking-human, 20 nonsmoking-human, 20 no-human-smoking, 20 no-human-nonsmoking) were then randomly paired, human-smoking with human-nonsmoking pictures and no-human-smoking with no-human-nonsmoking pictures.

In total, eight different picture sets were created as follows. This was accomplished by first creating 40 randomly paired picture sets. These were split into two sets of 20 picture pairs. Then the same pool of images was used to create another set of 40 randomly paired picture pairs which were again randomly sorted to create two more sets with 20 picture pairs each (same pictures, novel pairing). In all, four sets of 20 random picture pairs were created. To create eight sets we split each of the four existing

sets of 20 picture pairs in half to create eight sets of ten picture pairs. These sets were labeled A through H, and order of presentation of sets was randomized across participants (see **Table 4** for an example of how eight hypothetical participants were randomly assigned one of each picture set for each of the eight days of the study). **Figure 6** illustrates the creation of the eight sets of ten image pairings used in this study.

Participants were trained/assessed on each picture set for one "cycle" during the study. A cycle was defined as 3 trainings followed by 1 assessment. On any given cycle, participants received three AR or control trainings using a particular picture set (e.g., Set A), and attentional bias was assessed using the same set (in this example, Set A). On the next cycle, they were trained using a different picture set (e.g., Set B) and assessed using Set B. In this way the assessment of attentional used the materials on which participants had just received training. The first cycle was initiated by the first training after Visit 1. The first training (of a set of 3) occurred at different times of day over participants.

At the second laboratory visit, participants were assessed on a set of pictures which were randomly selected from the eight sets (the pictures were the same for each participant).

For the cued craving item, stimuli were eight pictures in landscape orientation that all contained smoking content. An example picture is shown in **Figure 4** and shows a group of people, some of whom are smoking and some who are not. At each assessment a picture was selected randomly for the cued craving assessment.

AR Condition

AR participants were scheduled to complete three modified VP tasks (attentional retrainings, 160 trials each) followed by one standard VP task (attentional bias

assessment, 80 trials) on each cycle on the PDA. Therefore, if subjects were compliant, the assessment occurred after 3 training tasks. In the modified VP the probe replaced the neutral picture on all (160/160) presented trials. Thus, there was a perfect correlation between picture type and dot location. In other respects, the AR task was identical to the standard VP task.

The number of trials presented for the AR (and Control) tasks (160) was selected to maximize the number of retraining trials presented, while not overburdening participants. In the pilot study of these procedures it was observed that the time to complete 160 trials was approximately 8 minutes and additional time requirements were seen as too cumbersome.

Control Training Condition

Control participants were scheduled to complete three control trainings (160 trials each) followed by one standard VP task (80 trials) per cycle on the PDA. The Control training tasks were identical to the assessment tasks with the exception of the number of trials presented. Field et al. (22) used this type of control condition as well as an "attend-alcohol" group in their AR study of alcohol users. In the Field et al. (27) study, the authors found that participants in the "attend-alcohol" group showed significantly elevated attentional bias for alcohol cues as well as a significant increase in alcohol craving after AR compared to the control group. For this reason we determined that an "attend-smoking" condition would be unethical as there is evidence that it could result in an increase in attentional bias, cigarette craving, and possibly cigarette smoking. Therefore, although the "attend-smoking" group may allow a stronger manipulation, we opted for the aforementioned control condition.

The benefits of this type of control condition are threefold. First, there will be no difference in duration of trainings between groups. Second, all participants will be equally practiced on the motor responses required for the task. Third, the same smoking and neutral pictures were presented with equal frequency to AR and control participants.

DATA REDUCTION AND ANALYSIS

On the standard VP task (292 assessments in the field), reaction times <100 ms were discarded (0.09% of trials). Median reaction times (correct responses) were used to reduce the influence of outliers. As noted earlier, attentional bias was computed as the difference in median reaction times to respond to probes that replaced smoking and neutral pictures. One bias extreme score (10.5 SD from mean) was removed, leaving 291 scores for analyses. The same methods were used for the laboratory assessments (standard VP task).

ANOVA (continuous variables) or Pearson's Chi Square test (categorical variables) were used to examine between-group differences at baseline.

To analyze the laboratory data we used ANCOVA, with one between-groups factor (Group: 2 levels, AR vs. control). ANCOVA is preferred to analysis of pre-post change scores when participants are randomly assigned to groups, and has greater power. Each dependent variable was tested in a separate model. Attentional bias assessed in the laboratory (hypothesis 1.1), QSU ratings (hypothesis 2.1), and cotinine/CO levels (hypothesis 3.1) served as the primary dependent variables. These variables were treated as continuous variables, and they were found to be approximately normally distributed.

To analyze EMA data, we used linear mixed models (LMM) analyses (PROC MIXED in SAS). These analyses accommodate different numbers of observations across

participants and can account for data clustering within individual participants. We used a random (subject-specific) intercept and an autoregressive model of order 1 for the residuals within subjects (all dependent variables). Day in study was entered as a continuous variable, along with Group and the Group by Day interaction term. If the interaction term was not significant it was dropped from the model. For the primary analyses, Day was treated as a fixed effect (the coefficients did not vary across participants). Attentional bias assessed on the PDA (hypothesis 1.2), and craving ratings assessed on the PDA (both cued and non-cued craving) (hypothesis 2.2) served as the primary dependent variables. We also used LMM to analyze daily smoking from the smoking diaries (hypothesis 3.2).

For analysis of lab and field data, baseline (pre-intervention) measures of the dependent variables (attentional bias, craving, smoking behavior) were included as covariates in the respective analyses. Each dependent variable was tested in a separate model. For primary analyses, parameter estimates (PE) (95% CI) from ANCOVAs and LMMs were reported as (unstandardized) measures of effect size (122). By aggregating over participants, Cohen's d was also reported for two primary outcome variables, attentional bias and cued craving.

Finally, to analyze the eye movement data (hypothesis 1.3) we used an independent samples t-test for continuous variables (e.g., gaze duration, number of gazepoints, number of fixations). The Satterthwaite t-test was applied if there was evidence that the variances differed between the two groups. As previously noted, analyses on eye movement data were conducted on 1) data from the first 5 seconds and 2) data from the first 60 seconds in which the participant was in the smoking lab.

For all tests, alpha was set to .05, and all tests were 2-tailed.

Eye tracking data reduction

As reported in **Figure 2**, eye tracking data were available from 24 participants (80.0%) in the AR group and 25 participants (83.3%) in the Control group. Data from the other participants were lost due to difficulties in calibration, equipment error, or researcher error.

As can be seen in **Table 7**, these 49 participants provided on average approximately 42 seconds of data from the 60 second task. One may wonder why there are not 60 seconds of data for each participant. There are a number of reasons for the loss of data. First, the Gazetracker software does not currently have the capability to identify blinks automatically. The average human blinks approximately every 4-5 seconds for approximately 300-400 ms for each blink cycle. Obviously, data are not recorded during a blink. Therefore, even under ideal conditions one would expect approximately 5 seconds of data to be missing due to blinks alone. Also, there are a number of challenges in mobile eye tracking with the monocle lens and specialized spectacles. The eye cannot be well tracked at the extremes of vertical or horizontal eye movements. Given that participants were walking into a room it is not surprising that their eyes likely scanned more than just straight forward as they entered the room. Also, there are a myriad of anatomical differences in eyes as well as other idiopathic factors which may make fitting, calibrating, and executing the eye tracking on these individuals more challenging (e.g., reticent to take off hat, bulky hair, etc.). Also, as previously mentioned, given the relatively modest digitization rate of mobile eye recording hardware, saccade

identification through saccade velocity detection is impossible. That is, saccades cannot be directly identified.

There is little peer reviewed evidence regarding how to implement a mobile eye tracking study such as this, and of those studies few discuss processing of data. Thus, there are no "standard operating procedures" for the processing of eye tracking data from the mobile eye tracker. However, it was obvious that there were large inter-individual differences in the amount of validly recorded data (e.g., some individuals had less than 10 seconds of validly recorded data for the 60 second sample). Therefore we determined that, in the primary analyses, we would limit analyses to those participants with greater than 30 seconds of data (for the 60 second sample), and 2.5 seconds (for the 5 second sample), who presumably provide more reliable data. In one thesis manuscript testing the ASL mobile eye system the authors had to drop 4/14 participants due to difficulties with calibration and other data handling errors (76). In the present manuscript, we lose 1 participant from the AR group and no participants from the control group for the first 5 seconds when we apply the "greater than 50%" rule. When we apply this rule to the 60 seconds sample we lose 5 from the control group and 2 from the AR group. Nonetheless, to provide a comprehensive report of the data we also report summary statistics and analyses using all participants (including those with less than 30 seconds of data).

Eye tracking results from the 60 second results were analyzed for internal consistency reliability by comparing number of recorded gazepoints within the smoking lookzone on "odd" seconds to those recorded on "even" seconds for participants with greater than 30 seconds of validly recorded data. Internal reliability was analyzed for each rater independently (rater 1: $n = 42$; rater 2: $n = 41$ – due to previously described

data loss as result of experimenter error). Internal reliability (split-half) was estimated using the Spearman-Brown correction (r*2/(1 + r)). It was excellent for both rater 1 (r = .95) and rater 2 (r = .94).

Power Analysis

Power Analyses were conducted using G Power Version 3. All power analyses assume alpha = .05 and a 2-tailed test.

For the laboratory data, assuming n = 30 in each group, a univariate two-group ANOVA with one between-groups factor (Group) will have power = .86 to detect a large effect size (d = 0.8 for the between-group difference at visit 2) and power = .48 to detect a medium effect size (d = 0.5).

For the EMA data, in the calculations described below, the power estimates account for the fact that repeated observations from the same person will be correlated, indexed by the intraclass correlation coefficient (ICC). Power estimates depend on both the size of the ICC and the average number of observations per person. These two factors are used to determine the variance inflation factor (VIF). The VIF measures by how much the total number of assessments must be reduced to yield an estimate of the "effective sample size" prior to use of the usual approaches to compute power. The VIF equals: 1+((average number of observations per person) -1)*ICC). The effective sample size is calculated using an estimate of the total number of assessments (i.e., average number of observations per person multiplied by the number of study participants) divided by the VIF. Assuming that participants complete 75% of the RAs scheduled per day, each participant will complete 0.75 VP assessments per day (= a total of 5.25 assessments per week). Thus, the estimated number of study assessments (not including

laboratory assessments) is 5.25 assessments x 30 participants x 2 groups = 315 assessments.

The power to detect a main effect of Group will decrease as a function of the correlation for the repeated measures. If the ICC = .1 (or .3), then the effective sample size = 220 (138), and we have power = .96 (.83) to detect a between-group difference of d = 0.5. The pilot data suggested that the effect size (d) for the effect of Group on attentional bias was greater than 0.5 after days 5 of the study.

CHAPTER 4: Results

AR (n=30) and Control (n=30) participants did not differ in terms of demographics assessed at Visit 1 (**Table 5**). They were of comparable age (F (1, 57) = 0.32, p =.58), gender (χ^2 (1, N=60) = 0.07, p =.80), and race (χ^2 (2, N=60) = 0.67, p =.72). They did not differ in terms of cigarettes smoked per day (F (1, 58) = 0.21, p =.65), FTND scores (F (1, 58) = 0.12, p =.73), lifetime quit attempts (F (1, 58) = 0.13 p = .72), or intent to quit (AR: 20% in next 30 days, 67% in next 6 months, and 13% not at all vs. Control: 27% in next 30 days, 60% in next 6 months, and 13% not at all, respectively; χ^2 (2, N=60) = 0.39, p =.82).

Participants were presented with a comparable number of RAs (a total of 735 in the AR group and 738 in the control group). They also responded to a similar percentage of presented RAs (79.1% in the AR group and 80.3% in the control group). The time of day that training assessments were presented was similar between groups with a mean time of 3:34 pm (SD = 3.54 hours) in the AR group and 3:04 pm (SD = 3.79 hours) in the control group. The mean time of day for completed attentional bias assessment tasks was similar between groups as well with a mean presentation time of 3:49 pm (SD = 5.04 hrs) in the AR group and 4.26 pm (SD = 5.02 hrs) in the control group. There was a total of 291 assessments completed with a mean duration of assessment tasks of 6.1 minutes (SD = 1.4). As a result of the increased number of trials on retraining and control tasks the mean duration of those tasks was higher at 8.4 min (SD = 2.3) for the retraining task and 8.4 minutes (SD = 1.3) for the control tasks. This difference was not significant between groups, F (1, 826) = 0.07, p =.79.

Participants in the AR condition (n = 29) completed a mean of 15.0 (SD = 3.6) AR tasks. Control participants (n = 30) completed a mean of 14.9 control tasks (SD = 3.4). Participants did not differ in the number of AR or Control tasks completed F (1, 56) = 0.35, p =.56. At the field assessment the mean time elapsed since preceding AR or Control task was 9.7 hr (SD = 8.9) and 7.9 hr (SD = 6.7), respectively, F (1, 230) = 1.84, p =.18. Similarly, there was no significant difference in number of AR or Control tasks completed prior to the field assessment in each cycle (2.74 (SD = 1.29) mean AR tasks and 2.70 (SD = 1.23) Control tasks) F (1, 234) = 0.12, p =.73. There was a mean duration of 18.7 hr (SD = 17.5) and 15.5 hr (SD = 12.6) from the preceding AR or Control task to the Visit 2 lab attentional bias assessment respectively, F (1, 56) = 0.47, p =.50.

Specific Aim 1: Effect of AR on Attentional Bias

Visual Probe Tasks

Participants committed a mean number of 0.4% (SD = 1.4) errors on field VP assessments in the field. **Table 6** includes summary statistics for field data.

Across both groups there was a significant attentional bias at baseline N = 60, M = 12.2 ms, SD = 37.5, t (59) = 2.53, p =.01. The two groups did not differ significantly at baseline in terms of attentional bias, F (1, 58) = 0.29, p =.68.

Regarding hypothesis 1.1, the effect of Group on attentional bias at Visit 2 was not significant when analyzed using ANCOVA with baseline attentional bias used as a covariate, F (1, 56) = 0.00, PE = -0.26, 95% CI [-20.8, 20.2], p =.98.

Regarding hypothesis 1.2, there was a significant Group x Day interaction F (1, 232) = 4.77, PE = 8.54, 95% CI [0.81, 16.3], p =.03 (**Figure 7**). This significant interaction persisted when controlling for time since last cigarette, F (1, 231) = 4.81, PE

= 8.61, 95% *CI* [0.88, 16.3], p =.03, and FTND scores, F (1, 232) = 4.72, *PE* = 8.51, 95% *CI* [0.80, 16.2], p =.03. In the AR group attentional bias decreased over time, F (1, 117) = 4.79, *PE* = -7.58, 95% *CI* [-14.4, -0.72], p =.03 but not in the control group, F (1, 115) = 0.16, *PE* = 0.92, 95% *CI* [-3.67, 5.51], p =.69. When analyzed over all days the control group exhibited a significant attentional bias towards smoking stimuli, t (28) = 2.37, *PE* = 10.9, 95% *CI* [1.49, 20.3], p =.02, but the AR group did not, t (27) = -0.43, *PE* = -3.26, 95% *CI* [-18.7, 12.2], p =.67. After Day 5 there was a significant difference between the two groups in attentional bias, F (1, 88) = 5.99, *PE* = 31.4, 95% *CI* [5.89, 56.8], p =.01 (d = 0.69). Despite this difference in attentional bias between groups after day 5, the AR group did not demonstrate significant attentional avoidance (negative attentional bias) after Day 5, t (27) = -1.76, *PE* = -17.6, 95% *CI* [-38.1, 2.87], p =.09.

Eye Tracking

Eye tracking data including summary and inferential statistics are presented in **Table 7** (all participants) and **Table 8** (participants in primary analyses).

As previously stated, we completed the primary analyses (reported below) using only those participants with greater than 50% of the total eye tracking time tracked in each of the two conditions (> 2.5 seconds for the 5 second analysis, > 30 seconds for the 60 second analysis). The 20 control participants and 22 AR participants with usable data for the 60 second clip did not differ in age, gender, race, cigarettes smoked per day, FTND scores, and lifetime quit attempts (all ps > .19). Similarly, the 20 control participants and 20 AR participants with usable data for the 5 second clip did not differ in age, gender, race, cigarettes smoked per day, FTND scores, and lifetime quit attempts (all ps > .21).

5-second clip

There was no significant effect of Group on time in the smoking zone, no. of gazepoints in the smoking zone, or number of fixations in the smoking zone. Given that there was evidence that the data were positively skewed, we recomputed all analyses using a non-parametric test, the Wilcoxon test. (The Wilcoxon test requires no assumptions about the shape of the distributions in the two populations). None of the findings presented in the top half of Table 8 changed when using the Wilcoxon test. For example, the p value for the between-group difference in the "total tracked time in smoking zone" was .13 using the t-test and .12 using the Wilcoxon test.

60-second clip

Consistent with hypothesis 1.3, the AR group gazed for a briefer duration within the smoking lookzone (M = 2.37 sec, SD = 1.81) than the control group (M = 4.37 sec, SD = 3.45), p = .03. Interpretation of this finding is complicated by the observation that, unexpectedly, there was a between-group difference in the total time tracked throughout the task (**Table 8**). The AR group had a briefer amount of time tracked than the control group, p = .03. It is not clear why the total time tracked should differ between the two groups. We therefore computed the percentage of time that was spent in the smoking zone (**Table 8**). The percentage of time spent within the smoking lookzone was marginally smaller in the AR group (5.33%, SD = 3.92) than the control group (8.81%, SD = 6.92), p =.056.

For the number of gazepoints measure, there was a significant main effect of Group for number of gazepoints recorded in the smoking lookzone with the AR group recording fewer gazepoints in the smoking zone (M = 61.48 gazepoints, SD = 48.67) than

the control group (M = 106.53 gazepoints, SD = 76.49), p = .03. Interpretation of this finding was straightforward because there was no between-group difference in number of gazepoints recorded over the entire task, and the finding was corroborated by the observation that a lower percentage of gazepoints of the AR group were in the smoking look zone (M = 5.96%, SD = 4.14), compared to the control group (M = 9.80%, SD = 7.18), p =.04.

For the number of fixations measure, the AR group had marginally fewer fixations in the lookzone than the control group (p = .09). However, interpretation is not straightforward because the AR group also had marginally fewer fixations overall, and there was no between-group difference in the percentage of fixations on smoking stimuli.

In sum, consistent with hypothesis 1.3, there was some evidence that AR participants spent less time looking at the smoking stimuli during the mobile eye tracking task.

Specific Aim 2: Effect of AR on Craving

Between-group differences in cued craving were not significant at baseline F (1, 58) = 0.30, p =.59.

Regarding hypothesis 2.1, using ANCOVA there was no effect of Group on cued craving, F (1, 56) = 0.22, PE = -0.25, 95% CI [-1.30, 0.81], p =.64, non-cued craving, F (1, 56) = 0.47, PE = -0.34, 95% CI [-1.32, 0.65], p =.50, or the QSU total score, F (1, 57) = 0.19, PE = 0.22, 95% CI [-0.78, 1.22], p =.66 at Visit 2.

Regarding hypothesis 2.2, there was no Group x Day interaction on cued craving when analyzed with LMM, F (1, 232) = 0.00, PE = -0.004, 95% CI [-0.21, 0.20], p =.96 (**Figure 7**, lower graph). There was a significant main effect of Group in the reduced

model (excluding the interaction term), F (1, 234) = 3.89, PE = 0.77, 95% CI [0.00, 1.55], p =.04; The AR group demonstrated significantly lowered cued craving (between-group difference in cued craving, d = 0.56) (**Figure 7**). However, there was no main effect of Group, F (1, 233) = 1.05, PE = 0.41, 95% CI [-0.38, 1.20], p =.31 on the non cued craving question. There was no Group by Day interaction, F (1, 232) = 0.06, PE = -0.025, 95% CI [-0.23, 0.18], p =.81 on the non cued craving item. The main effect of Group on cued craving persists when controlling for non-cued craving, F (1, 233) = 6.23, PE = 0.42, 95% CI [0.09, 0.74], p =.01, and when controlling for time since last cigarette, F (1, 231) = 5.64, PE = 0.41, 95% CI [0.07, 0.74], p =.01, and FTND scores, F (1, 232) = 6.61, PE = 0.43, 95% CI [0.10, 0.75], p =.01.

Specific Aim 3: Effect of AR on Smoking

AR participants reported smoking 13.5 (SD = 7.3) cigarettes per day on the smoking diary. Control participants reported smoking 13.7 (SD = 6.7) cigarettes per day. On the CO measure of smoking behavior, there was no significant between group difference at baseline, F (1, 58) = 0.03, p = .86. Similarly, there was no between group effect on cotinine, F (1, 58) = 0.21, p =.65 at baseline.

Regarding hypothesis 3.1, salivary cotinine levels at Visit 2 were not significant between groups when analyzed using ANCOVA, F (1, 57) = 0.33, PE = -23.4, 95% CI [-105.4, 58.6], p =.57. Similarly, CO levels at Visit 2 did not differ between groups using ANCOVA, F (1, 57) = 0.49, PE = -1.07, 95% CI [-4.13, 1.99], p =.49.

Regarding hypothesis 3.2, LMM analysis revealed no significant effect of Group on cigarettes smoked per day, F (1, 360) = 0.00, PE = 0.02, 95% CI [-1.84, 1.90], p =.98, nor a Group by Day interaction, F (1, 359) = 3.40, PE = -0.30, 95% CI [-0.62, 0.02], p

=.07. Although the Group by Day interaction was not significant, we calculated the effect of Day for each Group. The effect of Day was not significant for AR participants, PE = 0.12, SE = 0.13, p =.32 or for Control participants PE = -0.18, SE = 0.10, p =.07.

SENSITIVITY ANALYSES

We conducted supplementary analyses to determine the robustness of the presented findings.

Influence of Interruptions

First we examined the influence of interruptions on VP task performance. The percentage of reported interruptions during the VP task (AR vs. Control) were as follows and did not differ by Group (p =.96): No times = 58.2% vs. 56.7%; 1 time = 19.2% vs. 20.0%; 2 times = 14.4% vs. 11.7%; 3 times = 2.7% vs. 6.9%; 4+ times = 2.8% vs. 4.8%. We would expect reaction times for assessments with more interruptions to be slower as participants are distracted from task performance. Average reaction times on the VP task were as follows: No interruptions (n=167, M = 787.0 ms, SD = 217.3); 1 interruption (n=57, M = 747.8 ms, SD = 202.9); 2 interruptions (n=39, M = 881.0 ms, SD = 427.4); 3 interruptions (n=14, M = 881.2 ms, SD = 413.5); 4+ interruptions (n=15, M = 987.0 ms, SD = 770.7). As expected, assessments with more reported interruptions tended to have slower reaction times (and larger SDs): Using LMM, number of reported interruptions was associated with slower overall reaction time (PE = 39.7, SE = 14.0, p = .005). (No. of reported interruptions was not significantly associated with attentional bias, p = .15). When the 15 assessments with 4+ interruptions were excluded from analyses (the slowest and presumably the most unreliable assessments), the p value for the Group x Day became smaller, PE = 9.85, 95% CI [2.69, 17.0], p =.007. When analyses were subset to

the 224 assessments with no more than 1 interruption, the *p* value for the Group x Day was also smaller, *PE* = 7.17, 95% *CI* [1.72, 12.49], *p* =.01.

No. of interruptions appeared to exert an influence on the estimated intraclass correlation coeffificent (ICC) for attentional bias. The ICC, which varies between 0 and 1, is a measure of the proportion of variability in a variable that is accounted for by differences between subjects. If the ICC is high (the data are highly correlated), most of the variability is due to between-subject differences. If it is low, most of the variability is due to within-subject changes. When the ICC for attentional bias was assessed using all 291 assessments, the estimated ICC was very low (0.01). When the ICC was estimated using the 224 assessments with no more than 1 interruption, the estimated ICC (for attentional bias) was much higher (0.22). The estimated ICC for cued craving was 0.37 (calculated using 291 assessments). In future analyses we will examine the extent to which interruptions influence reliability assessed across assessments or within assessments.

Influence of Attentional Bias Outliers

When attentional bias scores at least as extreme as -321 ms and +255.5 ms were removed (corresponding to the 1% and 99% percentiles), leaving 286 assessments for analysis, the Group by Day interaction was significant, *PE* = 9.05, 95% *CI* [2.60, 15.4], *p* =.006. When attentional bias scores at least as extreme as -98.5 ms and +82 ms were removed (corresponding to the 5% and 95% percentiles), leaving 262 assessments for analysis, the Group by Day interaction was significant, *PE* = 4.01, 95% *CI* [0.32, 7.70], *p* =.03. Therefore, the Group by Day interaction was not caused by a small number of extreme scores.

Influence of Errors

As noted earlier, errors on the task were rare, and 99.3% of assessments (289/291) had 4 errors (5.0% error rate) or fewer. When analyses were conducted excluding the 2 assessments with greater than 4 errors, the *p* value for the Group x Day interaction became smaller, *PE* = 10.2, 95% *CI* [3.00, 17.4], *p* =.006.

Intent-To-Treat Analyses

The primary analyses used data from the 60 protocol completers (**Figure 2**). We also conducted intent-to-treat analyses using all available data. For lab data, this included all 65 participants who were randomized to treatment condition at visit 1, including 1 participant who did not receive trainings, the 3 protocol violators (who on average had a lag of 16.7 days between visit 1 and visit 2), and the participant who did not show for visit 2. For participants with missing data at Visit 2, Visit 1 data were used at that timepoint. Analyses of field data used the 60 participants with available data (including the 3 protocol violators). Results of these intent-to-treat analyses did not differ from analyses of protocol completers. For example, the Group x Day interaction for attentional remained significant, *PE* = 8.23, 95% *CI* [0.74, 15.7], *p* =.03.

Non-Linear Effects of Day

The analyses have so far examined the Group by Day interaction by treating Day as a linear variable. We also examined non-linear effects of Day on attentional bias and cued craving by testing the Group by Day Squared interaction term. (Day Squared was also included in these models). The Group by Day Squared term was not significant for either attentional bias, *PE* = -0.55, 96% *CI* [-4.23, 3.12], *p* = .76, or cued craving, *PE* = 0.02, 96% *CI* [-0.08, 0.12], *p* = .68.

Random Slope Models

In the previously reported analyses the coefficients of the slopes (over days) were treated as fixed rather than being allowed to vary across participants. We examined the results of analyses when the slopes were allowed to vary (random intercept and random slope models). Use of random slopes did not influence the main effect of Group on cued craving, which became slightly stronger, *PE* = 0.81, 95% *CI* [0.06, 1.56], $p = .03$. As before, there was no evidence for a Group by Day interaction, $p = .94$. When analyzing attentional bias, inclusion of random slopes did, however, reduce the Group by Day interaction to non-significance, *PE* = 6.74, 95% CI [-2.68, 16.11], $p = .16$. In the reduced model (excluding the non-significant interaction term), the main effect of Group was significant, *PE* = 18.3, 95% *CI* [4.01, 32.7], $p = .01$, meaning that, over all assessments, the AR group had lower attentional bias than the Control group. The effect of Group remained robust after day 5, *PE* = 21.8, 95% *CI* [7.4, 36.2], $p = .004$.

The above analyses were conducted without centering the predictors. We also centered the Group variable and Day variable, the latter using subject means rather than grand means. Analyses on centered predictors yielded similar results to those using noncentered predictors, with a significant interaction term when using fixed coefficients for Day ($p = .03$) and a p value of .13 for this interaction term when using random coefficients. When examining measures of model fit, the BIC values were similar in the fixed (3266.4) and random models (3265.6).

Although, as noted above, the Group by Day interaction was reduced to non-significance when random slopes were used, the interaction was significant or near-significant if assessments with large numbers of interruptions were excluded from analysis (e.g., when analyses were subset to the 224 assessments with no more than 1

interruption, the p value for the Group x Day was significant, $PE = 8.20$, 95% CI [0.66, 15.7], $p = .03$).

Effect of No. of Trainings Within-Cycle

As noted earlier, AR ($M = 2.74$, $SD = 1.29$) and Control participants ($M = 2.70$, $SD = 1.23$) completed a similar number of trainings within each cycle prior to the assessment. The effect of training might plausibly be larger at those assessments before which participants had received more prior trainings during the cycle. To examine this, we dichotomized no. of prior trainings into 1 or 0 prior trainings ("low" training) or 2 or more prior trainings ("high" training).

For attentional bias, the control group exhibited an attentional bias of 10.3 ms ($SD = 58.9$) and 11.9 ms ($SD = 50.1$) for the low and high training conditions respectively. The AR group exhibited an attentional bias of -0.1 ms ($SD = 85.2$) and -5.6 ms ($SD = 78.9$) for the low and high training conditions respectively. There was no Group by Training condition interaction ($p = .66$).

For cued craving, the control group reported cued craving of 4.00 ($SD = 2.08$) and 4.46 ($SD = 2.14$) for the low and high training conditions respectively. The AR group reported cued craving of 3.65 ($SD = 2.21$) and 3.75 ($SD = 2.26$) for the low and high training conditions respectively. There was no Group by Training condition interaction ($p = .75$). However, the effect of Group was significant for the high training condition ($p = .04$) but not the low training condition ($p = .21$).

Effect of AR on Cued Craving at Trainings

Due to software factors, the craving items were administered at trainings as well as assessments (n=886 trainings). The majority of these assessments occurred at the first

training (n=327 assessments) or second training (n=277 assessments) within a cycle, which was very different from the cued craving items at assessments (where only 39 out of 291 assessments occurred at the first or second position within a cycle). In contrast to the previously noted main effect of Group on cued craving at Assessments, PE = 0.77, 95% CI [0.00, 1.55], p = .04), a main effect of Group on cued craving was not observed at training assessments, PE = 0.21, 95% CI [-0.43, 0.85], p = .51). The difference in parameter estimates was statistically significant, Group x Assessment Type interaction, p = .03. It is possible that position in cycle accounts in part for the difference in findings. When analyses were restricted to data occurring after at least three trainings in the cycle, the pattern of data was more consistent, i.e., trainings, n=102, PE = 0.89, 95% CI [-0.22, 2.12], p = .11, and assessments, n=165, PE = 0.95, 95% CI [0.07, 1.84], p = .03, and not significantly different. An analysis of data (trainings and assessments) occurring after at least three trainings in the cycle yielded a similar result to the primary analysis, n=267, PE = 0.74, 95% CI [-0.00, 1.48], p = .05, which bolsters confidence in that result.

CHAPTER 5: Discussion and Conclusions

The major findings of this study were as follows. First, as hypothesized, AR delivered using a PDA in the natural environment reduced attentional bias to smoking cues over time when assessed in the field. Second, there was some evidence that AR reduced attentional bias assessed using eye tracking measures in the lab, but there was no evidence that AR reduced attentional bias assessed using the VP task in the lab. Third, consistent with hypothesis, AR reduced craving following a smoking cue when assessed in the field. AR did not reduce craving assessed in the lab. Last, there was no evidence that AR reduced smoking in this sample of non-treatment seeking smokers. All these findings will be discussed in greater detail below.

Effect of AR on Attentional Bias

Regarding the first aim, as previously noted there is evidence that AR administered in the field reduced attentional bias to smoking cues over time. This was evident in the significant decrease in attentional bias in the AR group over the week of the study. Interestingly, the reduction in attentional bias towards smoking cues did not appear to occur immediately. Rather, the effect became evident after several days of training (**Figure 7**). Our retraining protocol administered multiple "doses" of AR in smaller increments than the single session AR studies previously described (e.g., 20). More retraining sessions, or more retraining trials in each training session, may be required for more rapid, and larger, reductions in attentional bias. In designing the present study we endeavored to assess attentional bias each day during training. The consequence of this design is that participants in the AR group experienced a significant "break" in their AR during the administration of the assessment VP task. Whereas during the

retraining tasks their attentional bias was presumably being modified, during the VP assessment task their attentional bias may have been somewhat "reset". Stated another way, for an AR participant completion of a VP assessment is the same as completing a (briefer) control training. Future research may use a design in which attentional bias is assessed solely at the lab visits (or at the end of training on the PDA and not throughout the duration of retraining).

Although between-group differences in attentional bias were observed when assessed using the VP task in the field, between-group differences were not present at the second lab visit using this task. A rationale for conducting the study in the field was to attempt to alter a smoker's attentional bias towards smoking cues in their natural environment. It is noteworthy that the AR group never experienced retraining in the laboratory, and this may have made it more difficult to detect an effect of AR in that setting. That is, it may be easier to detect an effect of AR when the assessment occurs in the same context as the training. This possibility suggests that AR may need to occur in as many settings as possible. Another possible explanation for the absence of an effect of AR at the lab session was that there was a longer lag between the previous training and the lab assessment than was the case for field assessments. Additionally, the stimulus materials used at the second lab assessment were materials randomly sampled from all possible stimuli and so attentional bias was not being assessed on the specific materials on which they had recently been retrained.

In contrast to the null effect observed for the VP task in the lab, there was some support that attentional bias assessed using eye tracking measures was reduced by AR. The eye tracking outcome measures were exploratory, and there were considerable

challenges in data capture and analysis. That said, when analyses were conducted on participants with at least 30 seconds of data, AR participants looked at the smoking stimuli for a briefer period of time than the control group. This was true for both the time tracked measure (in seconds) and the number of gazepoints measure (Table 8).

If this finding is taken at face value, one may question why an effect of AR was observed on the eye tracking measure in the lab (at visit 2), but not on the VP task (at visit 2). There are a number of possible explanations for this finding. First, this may be due in some part to the observation by Field et al. (23) that eye tracking (specifically, dwell time) is a more sensitive measure of attentional bias than reaction time measures (such as the VP task). Second, the eye tracking measure was arguably a more ecologically valid measure of attentional bias than the VP task, and the set up on the study may have more closely resembled the context of training. Third, the eye tracking measure was only administered at visit 2 whereas the VP task was administered both at visit 1 and in the field. Therefore method differences may complicate interpretation of the comparison between the eye tracking measures and the VP task.

Effect of AR on Craving

Regarding the second aim, that AR would reduce cigarette craving in response to smoking cues, there was mixed support. Smokers in the AR group exhibited a significant overall reduction in cue-provoked craving assessed on the PDA after presentation of the cue stimulus. We hypothesized that after sufficient AR, smokers would attend less to smoking content relative to the neutral content during presentation of the cue stimulus and would therefore experience less cue-provoked craving compared to the control group. However, when considering the relationship between craving and attentional bias posited

by Franken (27), one might have expected cue provoked craving to change over time in the manner that attentional bias changed over time. However, although here was a main effect of Group in these analyses, there was no Group by Day interaction. However, this pattern of data is partially consistent with the findings in the AR for appetitive behaviors literature. Similar to the meta-analysis of AR in anxiety by Hakamata et al. (33), who observed that the number of retraining trials completed by participants significantly moderated the relationship between retraining and attentional bias but did not moderate the relationship between retraining and subjective experience.

Effect of AR on Smoking Behavior

Finally, regarding the third aim, that AR would reduce smoking behavior more than control training, there was no support. While there were no statistically significant effects of AR on smoking behavior there was a non-significant trend for smoking to decrease over time in the Control group relative to the AR group (i.e., an effect that is opposite to the predicted effect). Previous studies of AR in smoking have not shown an effect of AR on smoking behavior (1, 20, 61). Despite an observed reduction in cued craving in the AR group over time the AR group did not exhibit a decrease in smoking behavior. These data suggest that an effect of AR on craving is not necessarily accompanied by an effect on smoking behavior (at least over the course of the week observed in the present study).

The null effect on smoking behavior as a result of AR as found in previous studies as well as the current study has potentially important implications for the clinical utility of AR in smokers. While AR may prove effective at reducing attentional bias for smoking cues and cue provoked craving, these changes must be shown to result in

changes in smoking behavior for AR to prove clinically relevant. In the current study, it is worth noting that the participants were non-treatment seekers and were therefore not motivated to reduce their smoking. The effect of AR on smoking behavior may be easier to detect in individuals who are trying to quit smoking.

LIMITATIONS

There were a number of limitations to this study. First, the study did not investigate whether the effect of AR on attentional bias on the VP task generalized to novel (untrained) materials or other reaction time measures of attentional bias such as the modified Stroop. Clearly, cognitive training will only be effective if the training generalizes beyond the specific task and materials used. However, there was an effect of AR on attentional bias assessed with eye tracking. This suggests that the effect of AR generalizes to a new task. In addition, there was an effect of AR on craving reported after presentation of the smoking cue stimulus. This suggests that the effects of AR did generalize to novel stimuli (because these images were not used for AR or control trainings).

Second, and in a related point, this study is the first AR study to utilize an eye tracking measure of attentional as an outcome measure but this innovation came with risks. For example, there are no previous lab studies testing whether AR can influence eye movements. There is only evidence that eye tracking can be used as a measure of attentional bias (i.e., 39). Furthermore, to our knowledge a mobile eye tracking outcome measure has never been used to assess attentional bias in addiction. Moreover, although we examined the first 5 seconds of data, we did not examine the effect of AR on eye gaze over time during the task. It will be interesting to examine whether any effect of AR is

more apparent earlier in the task, and this should be a priority for additional analyses. However, despite these concerns and despite the challenges with this methodology, given the interesting results of our mobile eye tracking task future research should explore the utility of a mobile eye tracking measure of attentional bias in addiction.

Third, the sample size in this study was relatively small which resulted in low power to detect small and medium effect sizes on laboratory measures. However, for EMA data there were a larger number of observations available for analysis due to daily assessments for each participant which lead to higher power to detect an effect of AR in those data.

Fourth, we recruited non-treatment seeking smokers which may have made changes in smoking behavior less likely. Future research should be conducted with smokers trying to quit.

Fifth, there were limitations with the craving assessments used on the PDA. The two craving assessments were not counterbalanced during lab and field assessments. The cue provoked craving question was always presented first and the non-cue provoked craving question was always presented later in the sequence. Therefore, strong comparisons between the two measures cannot be made. In addition to the absence of counterbalancing, the cue-provoked craving question was developed for this study and has not been previously validated. Also, we do not know whether an effect of AR on the cue-provoked craving measures assessed on the PDA actually generalizes to naturally encountered smoking cues.

Sixth, participants did not record smoking behavior on the PDA which may have been more accurate than the smoking diaries. Given that participants had to complete 3

trainings and 1 assessment per day, we did not want to overburden them by asking them to make an entry on the PDA every time that they smoked. The daily paper smoking diaries were considered more user-friendly. Diary data were available for all participants, although this doubtless reflects in part "parking lot compliance". With our methods, any subtle effect of AR on smoking behavior may have been more difficult to observe.

Seventh, the study used multiple dependent variables in the lab and the field, and we did not correct for multiple tests. For example, attentional bias was assessed both in the lab and field, and three measures of craving were used (2 craving items on the PDA, and the QSU). Similarly there were multiple measures of smoking behavior (cigarettes smoker per day, cotinine levels in saliva, CO in breath). Therefore the type I error rate is elevated. However, for the primary outcome variables of attentional bias and craving both theory and data allowed for clear predictions to be made which somewhat obviates this concern. Nonetheless, replication of these findings is required to bolster confidence in their validity.

Eighth, this study did not assess the causal mechanisms linking attentional bias, craving, and smoking behavior. Further research on these mechanisms using multi-level mediation analyses is required (53). For example, it would be interesting to examine the association between attentional bias and craving, and to examine whether an effect of AR on craving was mediated by attentional bias (or vice versa). Given that AR appears to influence cued craving before (rather than after) it influences attentional bias (**Figure 7**), it seems unlikely that the effect of AR on cued craving will be mediated by attentional bias. Nonetheless, this needs to be formally examined. In future research it would also be

useful to assess craving after the eye movement task to see if reduced gaze duration on smoking stimuli results in lower craving ratings.

Ninth, as has been acknowledged elsewhere (115), we do not know the accuracy of reaction times assessed using this platform. Any inaccuracy in assessment of reaction time will of course negatively influence the quality of the attentional bias data (but see 110, for estimated split-half reliabilities of .96 or greater for reaction times on this platform). Also, it would have been useful to assess task irritation (as well as reported interruptions) after each VP task, to examine if task irritation influences the reliability of data.

Finally, this study focused on the retraining of only one sensory modality. All prior studies of AR have used visual attention retraining strategies. However, it is clear that other sensory modalities are important and presumably in competition for cognitive resources. Cigarette smokers are likely to have their attention grabbed by the smell of cigarette smoke just as they are likely to have their attention grabbed by the sight of someone smoking. Other AR techniques may be developed to retrain other sensory modalities. This point may be particularly relevant for the eye movement part of the study because the cigarette may attract an individual's attention through its smell (even though it was not lit). Future studies will be required to determine whether AR procedures are applicable to other modalities.

STRENGTHS

The study also had strengths. First, this is the first study to report the use of an AR intervention administered on a mobile device in the natural environment. Second, the study was the first to report the changes in attentional bias over time during an AR

protocol. Third, the study was the first to use eye tracking measures to examine the impact of AR.

Future Directions

Given that the effect of AR became more pronounced over time, it would be interesting to extend the duration of training to examine if an effect continues to get larger over time. In particular it would be interesting to observe whether significant avoidance of smoking cues can be obtained (i.e., faster responses to probes that replace neutral vs. smoking stimuli). It would also be informative to further examine the extent to which effects of AR generalize to new stimuli and new tasks. Regarding experimental parameters, Field and Cox (19) argue that stimulus onset asynchrony (SOA) in attentional bias research of 200 ms assesses initial orienting and SOA of 500 ms or more also assesses delayed disengagement. Therefore, another possible avenue of research is to manipulate the SOA to examine if AR can be observed as alterations in initial orienting (e.g., 200 ms) as well as disengagement (500 ms as used here). Finally it will be important to investigate whether AR can reduce smoking or relapse in smokers trying to quit. As noted above, we are not aware of any AR study in tobacco addiction that has reported a reduction of smoking behavior or relapse. Given that a reduction of smoking behavior is the primary target of AR, it will be critical to conduct studies using a treatment-seeking population.

There is also significant opportunity to adapt AR in ways which may improve compliance with training. Regarding compliance, it was anecdotally noted by some participants in the current study that AR tasks are boring. Wiers et al. (121) has suggested adapting the existing AR tasks to include elements similar to video games

("gamification") wherein decreased attentional bias is rewarded in some way. Similarly, insights from contingency management approaches to drug addiction may be useful to increase compliance (see 72).

Another issue requiring investigation is the role of explicit instruction – i.e., whether it would be beneficial to inform participants as to the contingencies at the outset of the study. This idea has been noted in the literature (e.g., 54) but we are not aware of any studies that have manipulated "contingency knowledge" as an independent variable. It is possible that explicit instruction on the contingencies would be beneficial for AR, although MacLeod et al. (54) note that there are potential downsides. For example, there is evidence that instructing participants to avoid processing certain types of information can have a paradoxical or "ironic" effect of increasing its processing (117). In the current study, we assessed whether AR participant became aware of the contingencies during the study (at visit 2), but an analysis of role of contingency awareness in the AR group was beyond the scope of the dissertation. Further research is required on the role of explicit instruction on AR.

More broadly, if such studies reveal that AR may be useful, then AR might be combined with other interventions to further improve smoking cessation interventions (95). For example, pharmacologic interventions have been used successfully in the treatment of some addictive behaviors (74). However, there is growing interest in medications to improve cognitive functioning in drug addicted individuals (95). Specifically, medications shown to improve executive functioning (i.e., working memory) such as modafinil (e.g., 15) could be combined with AR to examine possible combination therapies in addiction treatment. Similarly, AR could be combined with

other cognitive training tasks designed to improve cognitive functioning (e.g., 48). These possible approaches to improving the effectiveness of interventions for addiction are in line with the aforementioned dual-process model of drug use and addiction (see also 106).

Strategies could also be used to improve ease and timeliness of AR interventions. For example, the training could be adapted as a smartphone based mobile application to allow for ease of access among smartphone users. Mobile applications could be programmed to allow for user initiated or regularly scheduled attentional bias assessment tasks which could prompt the delivery of AR in situations when attentional bias is elevated (e.g., see 110). Affective states which increase risk of relapse could be assessed in real-time and an intervention delivered when needed. In addition, global positioning functionality in smartphones could monitor users' locations to self-identified "hot-spots" in their environment. Ultimately it may be possible to develop an algorithm that links cognitive, affective, and environmental variables to risk of relapse, and to deliver AR and other interventions at the very time when it is most beneficial ("ecological momentary interventions") (see 62 for a review of the potential of smartphones to monitor risk and deliver interventions).

Finally, the current study was a trial of retraining visual attention only. This is only one modality of a multi-modal attentional system. That is, other sensory modalities of attention may be susceptible to retaining. It is possible that tasks based on the AR intervention described here could be developed to retrain auditory or even olfactory attention. An important first step in this process would be the exploration of possible attentional biases for addictive cues in these modalities. Addicted individuals may be

found to orient preferentially towards sounds or discussions related to addictive cues. They may also attend preferentially to odors associated with addictive substances and cues (i.e. the smell of cigarette smoke). If these attentional biases were observed it may be possible to reduce these biases through repeated exposure to addictively salient cues (odors or sounds) in the presence of neutral cues in a task which requires rapid attentional orienting towards the neutral cues. As an example, participants could be asked to identify a pleasant or neutral odor presented simultaneously with the odor of cigarette smoke. Their instructions would be to identify the neutral odor as quickly as possible.

SUMMARY

In summary, multiple sessions of AR delivered on a PDA in a cigarette smoker's natural environment can reduce attentional bias to smoking cues. There was some evidence that AR may have an effect on cue-provoked craving, but further research is required to bolster confidence in this finding. There was no support that the AR protocol used here reduces smoking behavior in a sample of adults not currently attempting to quit. Finally, a mobile eye tracking measure of attentional bias may be a promising new method to assess naturalistic attentional bias for smoking cues.

Table 1: Summary table of eye tracking studies in the addictions.

Study	Participants	Eye Tracking Task	Fixation Definition	Independent Variables	Main Outcome Variables	Main Findings
Weafer and Fillmore, 2013 (116)	40 moderate to heavy alcohol drinkers	Visual probe task	stable within 0.5^0 for >100ms	Drinking status (heavy, moderate); Alcohol prime (placebo, 0.45 g/kg body weight, 0.65 g/kg body weight) Picture type during VP task (alcohol, neutral)	Attentional bias (VP – calculated from mean fixation times); Desire for Alcohol (DAQ); Alcohol consumption (Ad Lib alcohol task)	**Attentional Bias:** Group by Image by Dose interaction with significant main effect of Image (towards alcohol) and Dose (decreased AB in heavy drinkers with increasing Dose). **Desire for Alcohol:** Main effect of Dose only with increased desire with increased dose. **Ad Lib Alcohol:** Main effect of Group with Heavy > Moderate.
Rose et al., 2013 (80)	64 student social drinkers	Operant choice task (alcohol or non-alcohol related reward choice presented)	stable within 1^0 for >100ms	Alcohol devaluation (No devaluation = unadulterated alcohol, Devaluation = adulterated alcohol to taste unpleasant), Reward choice (alcohol image, non-alcohol image)	Behavioral choice (Operant choice task), Gaze dwell time, Initial fixation, Final fixation	**Behavioral Choice:** Alcohol devaluation by Time with reduced preference for alcohol reward in devaluation group only from pre to post task. **Dwell Time:** Alcohol devaluation by Reward choice interaction with devaluation group only with less dwell time on alcohol image from pre to post task. **Initial Fixation** Alcohol devaluation by Reward choice interaction with only devaluation group with less frequent initial fixations on alcohol image from pre to post task. **Final Fixation** Alcohol devaluation by Reward choice interaction with only devaluation group with less frequent final fixations on alcohol image from pre to post task.
Miller and Fillmore, 2010 (63)	25 adult alcohol drinkers	Visual probe task	stable within 0.5^0 for >100ms	Picture type during VP task (alcohol, neutral); Image complexity (simple, complex)	AB-RT (VP), AB: Fixation duration (eye-tracking during VP); Drinking habits (12 week TLFB)	**AB – Reaction Time:** Picture type by Image complexity interaction with faster RT to simple alcohol images than complex alcohol images. No effect of Picture type within complex images. **AB – Fixation duration:** Picture type by Image complexity interaction with longer fixation durations on simple alcohol images than complex alcohol images. No effect of Picture type within complex images. **Drinking habits:** Increased AB-Fixation duration predicted increased drinking habits over prior 12 weeks. Non-significant trend in AB-RT.
Schoenmakers et al., 2008 (85)	23 heavy social drinkers	Visual probe task	stable within 1^0 for >100ms	Alcohol prime (alcohol prime, placebo prime); Picture type during VP task (alcohol, control); Picture type during SRC task (alcohol, control)	AB (VP), Gaze dwell time, Initial fixation, Craving for alcohol (DAQ), Approach bias (SRC task)	**Attentional Bias:** Alcohol prime by Picture Type interaction with increased AB after an alcohol prime. No AB noted in placebo prime. **Dwell Time:** Main effect of Picture Type after alcohol prime with longer dwell time on alcohol images. No effect after placebo prime. **Initial Fixation:** Main effect of Picture Type after alcohol prime with alcohol images with more initial fixations. No effect after placebo prime. **Craving:** Time by Alcohol prime interaction with increased craving from pre-session to post-session in alcohol prime only. **Approach bias:** Main effect of Picture Type with increased approach bias towards alcohol regardless of prime condition.
Hogarth et al., 2008 (39)	32 contingency aware smokers	Static stimulus viewing	Unreported	Dual Task (Auditory and visual); Picture Type (paired with smoking, paired with neutral)	Total fixation count, Dwell time, Cigarette reward expectancy	**Total Fixation Count:** Main effect of Picture Type with higher fixations on paired with smoking before dual task; No effect after dual task **Dwell Time:** Main effect of Picture Type with longer dwell time on paired with smoking before dual task; No effect after dual task **Cigarette Reward Expectancies:** Main effect of Picture Type with longer dwell time on paired with smoking before dual task; No effect after dual task
Bradley et al.,	12 smokers, 12	Visual probe	stable within	Smoking status (Smokers,	Direction of initial	**Attentional Bias:** Main effect of Smoking status

2007 (6)	nonsmokers	task	1^0 for >100ms	Nonsmokers); Mood induction (negative, positive, & neutral)	fixation, Dwell time, AB (VP)	**Initial Fixation:** Mood Induction by Smoking status interaction with smokers in negative mood highest **Dwell Time:** Mood induction by Smoking status interaction with smokers in negative mood longest
Kwak et al., 2007 (49)	14 smokers and 16 nonsmokers	Static dual image viewing task	stable within 1^0 for >100ms	Smoking status (Nonsmokers abstinent smokers): Picture Type (aversive, smoking, neutral)	Direction of initial fixation, Dwell time, Anxiety (STAI)	**Initial Fixation:** Smoking status by Picture type interaction with smokers attending to negative stimuli first **Dwell Time:** Smoking status by Picture type interaction with smokers dwelling longer on smoking stimuli
Hogarth et al., 2006 (38)	16 smokers	static stimulus viewing	Unreported	Contingency awareness (aware, unaware), Picture Type (paired with smoking, paired with neutral)	Dwell time, Cigarette reward expectancy	**Dwell Time:** Contingency awareness by Picture Type with aware with longer on smoking paired stimuli **Cigarette Reward Expectancies:** Main effect of Contingency awareness with aware higher
Mogg et al., 2005 (66)	41 smokers	Visual probe task	stable within 1^0 for >100ms	Dependence (low, moderate), Picture Type (smoking, neutral)	Direction of initial fixation, Dwell time, Approach behavior (SRC)	**Attentional Bias:** Main effect of Dependence with low dependent with higher AB **Initial Fixation:** No effect **Dwell Time:** Dependence by Picture Type interaction with low dependent smokers higher **Approach Behavior:** Main effect of Dependence with low dependent higher
Field et al., 2004 (23)	23 smokers	Visual probe task	stable within 1^0 for >100ms	Smoking status (abstinent, non-abstinent), Picture Type (smoking, neutral)	Direction of initial fixation, dwell time, AB (VP)	**Attentional Bias:** No effect **Initial Fixation:** No effect **Dwell Time:** Main effect of Smoking status
Mogg et al., 2003 (65)	20 smokers, 25 nonsmokers	visual probe task	stable within 1^0 for >100ms	Smoking status (Smokers and nonsmokers), Picture Type (smoking, neutral)	Direction of initial fixation, Dwell time, Latency to fist fixation, AB (VP)	**Attentional Bias:** Main effect of Smoking status **Initial Fixation:** Smoking status by Picture Type interaction with smokers attending to smoking stimuli first **Dwell Time:** Smoking status by Picture Type interaction with smokers attending to smoking stimuli longest
Rosse et al., 1992 (81)	19 cocaine users	static visual scanning task	No fixations	Cocaine use (heavy, light): Picture Type (crack pipe, flower)	90 second visual scanning gestalt qualitative rating	**Gestalt Qualitative Rating:** Cocaine use by Picture Type interaction with heavier cocaine users visual scanning of crack pipe more complete than lighter users; Main effect of Picture Type with scanning of crack pipe picture more complete than flower.

Table 1 Note: Portions of table and text adapted from Kerst (47). AB = Attentional Bias; QSU = Questionnaire for Smoking Urges; QCU = Questionnaire for Cocaine Urges; RT = Reaction Time; SRC = Stimulus-response Compatibility task; STAI = State-Trait Anxiety Inventory; TLFB = Timeline Follow-back; VP = Visual Probe Task.

Table 2: Summary table of existing Attention Retraining literature in the addictions.

Study	AR Sessions	AR trials (Assessment trials)	Participants	AR Groups	Main Outcome Variables	Main Findings
McHugh et al., 2010 (61)	Single Session	Visual Probe: 476 (276)	51 Current smokers	Attend-Smoking vs. Avoid-Smoking	Attentional Bias (VP); Craving (QSU-Brief)	**Attentional Bias** (VP): No effect. **Craving** (QSU-Brief): No effect
Schoenmakers et al., 2010 (87)	Five Sessions	Visual Probe: 2.640 (216)	33 inpatient and 10 outpatient abstinent alcoholics	Avoid alcohol vs. categorization control task	Attentional Bias (VP); Craving (DAQ); Months to relapse; Time to discharge from inpatient	**Attentional Bias** (VP): Simple effect of group at post-training. **Craving** (DAQ): No effect **Months to Relapse:** AR group 1.25 months longer to relapse **Time to discharge from inpatient:** AR group discharged an average 28 days earlier
Field et al., 2009 (20)	Single session	Visual Probe: 1,792 (320) Pictorial Stroop: NA (160)	72 Current smokers	Attend-Smoking vs. Avoid-Smoking	Attentional Bias (VP and Stroop); QSU – Brief, Tobacco Seeking (willingness to pay delay discounting)	**Attentional Bias** (VP): Group by Time interaction at second session for trained but not novel stimuli. **Attentional Bias** (Pict. Stroop): No effect **Craving** (QSU): Main effect of time. **Tobacco Seeking:** No Effect
Fadardi and Cox, 2009 (18) Sample 2	2 sessions, 1 week apart	Pictorial Stroop: Not reported Emotional/ Classic Stroop: (384)	68 Hazardous drinkers	Avoid-Alcohol	Attentional Bias (Alcohol, Concern, Classic Stroop tasks); Motivation to Change (RTCQ)	**Attentional Bias**: Stroop Type by Time interaction: reduction in interference on Alcohol and Classic but not Concern Stroop from prêt-training to post-training **Craving** Not assessed **Motivation to Change** Heaviest drinkers showed increased motivation to change their drinking behavior
Fadardi and Cox, 2009 (18) Sample 3	4 sessions, 1 per week for 2 4 weeks	Pictorial Stroop: Not reported Emotional / Classic Stroop: (768)	92 Harmful drinkers	Avoid-Alcohol	**Attentional Bias** (Alcohol, Concern, Classic Stroop task); Motivation to Change (RTCQ), Alcohol Consumption (TAAD)	**Attentional Bias**: Stroop Type by Time interaction: reduction in interference on Alcohol and Classic but not Concern Stroop from Baseline to post-training but not from post-training to 3 month follow-up **Craving** Not assessed **Motivation to Change** Main effect of Time. **Alcohol Consumption** Main effect of Time - decrease in consumption at post-training.
Attwood et al., 2008 (2)	Single session	512 (256)	55 Current smokers	Attend-Smoking vs. Avoid-Smoking	Attentional Bias (VP); QSU – Brief, VAS; Smoking topography	**Attentional Bias** (VP): Group by Time interaction. **Craving** (QSU): Group by Time interaction for males but not for females. In males: change in AB across training correlated with change in craving across cue exposure. **Smoking Topography**: No effect
Field et al., 2007 (22)	Single session	960 (1,724)	60 Heavy social drinkers	Attend-Alcohol vs. Avoid-Alcohol vs. Control	Attentional Bias (VP + Alcohol Stroop); SRC Task; Urge to drink, DAQ; Alcohol consumption (Alcohol vs. Orange Juice)	**Attentional Bias** (VP): Group by Time interaction. Alcohol Stroop: No effect **Craving** (Urge to drink): Time **Alcohol Consumption** No effect
Schoenmakers et al., 2007 (86)	Single session	624 (100)	106 Heavy drinkers	Avoid-Alcohol vs. Control	Attentional Bias (VP); Craving; Drink choice task (soda vs. beer)	**Attentional Bias** (VP): Group by Time interaction. **Craving** No effect **Drink Choice** No effect
Field and Eastwood, 2005	Single session	896 (126)	40 Social drinkers	Attend-Alcohol vs.	Attentional Bias (VP); DAQ, ACS, Urge to drink,	**Attentional Bias** (VP): Group by Time interaction; attend-alcohol group significant increase over time, avoid-alcohol

Study	AR Sessions	AR trials (Assessment trials)	Participants	AR Groups	Main Outcome Variables	Main Findings
(21)				Avoid-Alcohol	alcohol; Alcohol consumption (Beer vs. Orange)	group significant decrease over time. **Craving** (Urge to drink): Group by Time interaction, attend-alcohol group increased over time. **Alcohol Consumption**: attend-alcohol group consumed significantly more beer.

Table 2 Note: Portions of table and text adapted from Kerst (47). AB = Attentional Bias; AR = Attentional Retraining; DAQ = Desire for Alcohol Questionnaire; QSU = Questionnaire for Smoking Urges; SRC = Stimulus-response Compatibility task; VAS = Visual Analog Scale; VP = Visual Probe Task. In the single session studies, the outcome variables were assessed before and after AR.

Table 3: Summary of Study Procedures.

	Phone Scr.	Visit 1 0	Day 1	2	3	4	5	6	Visit 2 7
Modality/Location of Contact	Phone	USUHS							USUHS
Inclusion/Exclusion Criteria	X	X							
QUESTIONNAIRE ASSESSMENTS									
Demographics		X							
Smoking History		X							
FTND		X							
BIDR		X							
QSU		X							X
Smoking Assessments (Diary)		X	X	X	X	X	X	X	X
BIOCHEMICAL ASSESSMENT									
Breath Sample for CO		X							X
Saliva Sample for Cotinine		X							X
INFORMED CONSENT									
Participant signs ICD		X							
Debriefing									X
Receipt of Compensation									X
RANDOMIZATION									
Assignment to AR or Control		X							
PDA TRAINING									
Participant receives training		X							
LAB ASSESSMENTS									
Standard VP Task		X							X
Mobile Eye Assessment									X
TRAININGS									
AR or Con (3 RAs per cycle)		X	X	X	X	X	X	X	X
FIELD ASSESSMENTS									
1 RA per cycle		X	X	X	X	X	X	X	X
COMPENSATION*									
Laboratory Sessions		$20							$20
Days contributing data		$5	$5	$5	$5	$5	$5	$5	
Each field assessment		$2	$2	$2	$2	$2	$2	$2	$2

Table 3 Note: Portions of table and text adapted from Kerst (47). FTND = Fagerstrom Test for Nicotine Dependence; QSU = Questionnaire for Smoking Urges; BIDR = Balanced Inventory of Desirable Responding; CO = carbon monoxide; VP = visual probe task; RA = Random

Assessments. (see Appendix A for questionnaires). *Non-federal civilians (see Appendix B for compensation procedures for federal civilians)

Table 4: Sample of the sets of stimuli used for eight participants over the course of the eight days of AR.

	Cycle							
	1	2	3	4	5	6	7	8
Participant 1	C	E	G	D	B	H	A	F
Participant 2	A	C	D	G	E	F	H	B
Participant 3	B	F	E	A	G	H	C	D
Participant 4	D	F	G	B	C	A	F	E
Participant 5	A	G	B	C	D	F	G	E
Participant 6	B	G	C	D	A	E	G	F
Participant 7	C	A	G	F	G	B	E	D
Participant 8	D	C	F	E	A	H	B	G

Table 4 Note: Portions of table and text from Kerst (47). Stimuli sets A – H are randomly ordered over the course of the eight cycles to minimize any potential carry-over effects. A cycle was defined as 3 trainings followed by 1 assessment.

Table 5: Demographic characteristics of Sample

	AR (n = 30)	Control (n = 30)
Participant Demographics		
Age	41.8 (10.2)	43.6 (14.0)
Sex	50.0% Female	46.7% Female
Race	20.0% White	16.7% White
	56.7% Black	66.7% Black
	23.3% Other	16.7% Other
Years of Education	12.50 (1.38)	13.67 (2.08)
Cigarettes per day	15.3 (8.5)	16.2 (7.4)
FTND (0-10)	5.4 (2.3)	5.2 (2.2)
Lifetime Quit Attempts (+24hrs)	5.3 (3.1)	5.0 (3.0)

Table 5 Note: Portions of table and text adapted from Kerst (47). Mean (SD) for Participant Demographics. FTND: Fagerstrom Test of Nicotine Dependence.

Table 6: Summary Statistics on Dependent Variables by Training Group and Day.

		Day								
		Base	1	2	3	4	5	6	7	Visit 2
AR	Attentional Bias (ms)	10.1 (36.8)	16.1 (33.7)	11.2 (116.9)	16.7 (26.0)	9.3 (61.4)	-23.1 (101.9)	-2.8 (57.6)	-22.6 (92.6)	-0.0 (46.1)
	Cued Craving (1-7)	4.53 (2.01)	4.25 (1.67)	3.37 (2.03)	4.48 (1.94)	2.90 (1.89)	3.88 (2.45)	3.35 (2.58)	3.91 (2.36)	3.83 (2.22)
	Non-Cued Craving (1-7)	4.83 (1.86)	3.50 (1.93)	3.68 (2.08)	4.48 (2.16)	3.29 (2.12)	4.00 (2.35)	3.60 (2.52)	3.94 (2.42)	3.90 (2.02)
	No. Cigs Smoked (Diary)		12.6 (7.2)	13.8 (7.9)	13.0 (7.9)	14.1 (7.0)	13.7 (9.2)	13.9 (7.5)	13.5 (8.0)	
	QSU Ratings (0-10)	5.05 (2.76)								3.84 (2.33)
	CO (ppm)	15.9 (5.35)								15.5 (7.70)
	Cotinine (ng/ml)	394 (181)								410 (211)
CON	Attentional Bias (ms)	14.4 (38.7)	-14.2 (52.5)	16.0 (48.6)	18.8 (39.3)	8.6 (31.1)	29.5 (62.6)	10.4 (30.1)	0.1 (72.0)	-0.3 (30.4)
	Cued Craving (1-7)	4.23 (2.22)	4.47 (1.85)	4.55 (2.28)	4.32 (2.01)	4.48 (2.13)	4.00 (2.21)	3.85 (2.23)	4.24 (2.14)	3.43 (2.24)
	Non-Cued Craving (1-7)	4.57 (2.18)	3.80 (2.14)	4.25 (2.27)	4.18 (2.13)	4.39 (2.15)	4.25 (2.29)	3.35 (2.16)	4.19 (2.16)	3.43 (2.21)
	No. Cigs Smoked (Diary)		14.1 (6.1)	14.4 (7.0)	15.1 (7.1)	14.8 (6.4)	13.8 (7.9)	13.3 (6.6)	13.3 (7.8)	
	QSU Ratings (0-10)	4.31 (2.86)								3.66 (2.45)
	CO (ppm)	15.6 (4.68)								14.2 (5.81)
	Cotinine (ng/ml)	420 (253)								408 (268)

Table 6 Note: Mean (SD) for Bias scores (ms), Craving, and other study measures. Base = baseline. Data for Base and Visit 2 are from laboratory sessions. Data from Days 1-7 derive from EMA assessments. Day 7 column includes EMA assessments occurring on day 8 (Visit 2 day) prior to the Visit 2. ns at baseline were 30 for AR and CON. ns for days 1-7 for the CON group were 15, 20, 22 23, 24, 20, 21. For the AR group ns were 8, 19, 21, 21, 25, 20, 32 for days 1-7 respectively.

Table 7: Mobile Eye tracking gaze duration and gazepoint data for all participants.

Mobile Eye Data

First 5 seconds	Control (n=20)	AR (n=21)	t	df
Total time tracked (sec)	4.41 (0.61)	3.84 (0.98)	2.25*	33.5
Total tracked time in smoking zone (sec)	1.19 (0.97)	0.70 (0.86)	1.69#	39
Percentage of tracked time in smoking zone (%)	26.25 (20.33)	17.07 (21.21)	1.41	39
Total Gazepoints (number)	108.55 (20.09)	99.10 (27.87)	1.24	39
Total Gazepoints in smoking zone (number)	33.20 (27.68)	20.19 (23.66)	1.62	39
Percentage of Gazepoints in smoking zone (%)	29.75 (21.67)	19.21 (21.83)	1.55	39
Total no. of fixations (number)	3.40 (2.35)	3.29 (1.98)	0.17	39
Total no. of fixations in smoking zone (number)	1.73 (1.74)	1.40 (1.81)	0.58	39
Percentage fixations in smoking zone (%)	43.00 (38.74)	38.38 (42.43)	0.36	39
First 60 seconds	Control (n=25)	AR (n=24)		
Total time tracked (sec)	42.03 (14.69)	41.50 (8.85)	0.15	47
Total tracked time in smoking zone (sec)	3.60 (3.48)	2.21 (1.82)	1.77#	36.6
Percentage of tracked time in smoking zone (%)	7.92 (7.51)	5.01 (3.92)	1.71#	36.5
Total Gazepoints (number)	949.92 (367.08)	968.46 (291.62)	-0.20	47
Total Gazepoints in smoking zone (number)	87.76 (78.73)	57.75 (48.44)	1.61#	40.1
Percentage of Gazepoints in smoking zone (%)	8.64% (7.57)	5.63% (4.16)	1.74#	37.6
Total no. of fixations (number)	46.28 (23.75)	43.08 (19.10)	0.52	47
Total no. of fixations in smoking zone (number)	5.32 (5.41)	3.65 (3.33)	1.31	40.1
Percentage fixations in smoking zone (%)	11.02 (12.88)	7.89 (6.62)	1.08	36.2

Table 7 Note: Mean (SD) of mobile eye tracking data. #p < .1, *p < .05

Table 8: Mobile Eye tracking gaze duration and gazepoint data for participants with greater than 50% of data validly recorded.

Mobile Eye Data

First 5 seconds	Control (n=20)	AR (n=20)	t	df
Total time tracked (sec)	4.41 (0.61)	3.98 (0.76)	1.98#	38
Total tracked time in smoking zone (sec)	1.19 (0.97)	0.74 (0.87)	1.54	38
Percentage of tracked time in smoking zone (%)	26.25 (20.33)	17.92 (21.39)	1.26	38
Total Gazepoints (number)	108.55 (20.09)	102.20 (24.59)	0.89	38
Total Gazepoints in smoking zone (number)	33.20 (27.68)	21.20 (23.81)	1.47	38
Percentage of Gazepoints in smoking zone (%)	29.75 (21.67)	20.17 (21.93)	1.39	38
Total no. of fixations (number)	3.40 (2.35)	3.40 (1.96)	0.00	38
Total no. of fixations in smoking zone (number)	1.73 (1.74)	1.48 (1.83)	0.44	38
Percentage fixations in smoking zone (%)	43.00 (38.74)	40.30 (42.59)	0.21	38
First 60 seconds	Control (n=20)	AR (n=22)		
Total time tracked (sec)	48.27 (7.76)	43.22 (6.83)	2.24*	40
Total tracked time in smoking zone (sec)	4.37 (3.45)	2.37 (1.81)	2.32*	28.2
Percentage of tracked time in smoking zone (%)	8.82 (6.96)	5.33 (3.92)	1.98#	29.3
Total Gazepoints (number)	1,086.55 (262.35)	1,000.59 (274.40)	1.04	40
Total Gazepoints in smoking zone (number)	106.53 (76.49)	61.48 (48.67)	2.25*	31.7
Percentage of Gazepoints in smoking zone (%)	9.80% (7.18)	5.96% (4.14)	2.10*	29.8
Total no. of fixations (number)	55.00 (17.39)	45.32 (18.30)	1.75#	40
Total no. of fixations in smoking zone (number)	6.35 (5.47)	3.95 (3.31)	1.70#	30.7
Percentage fixations in smoking zone (%)	11.05 (9.18)	8.51 (6.56)	1.04	40

Table 8 Note: Mean (SD) of mobile eye tracking data. #p < .1, *p < .05

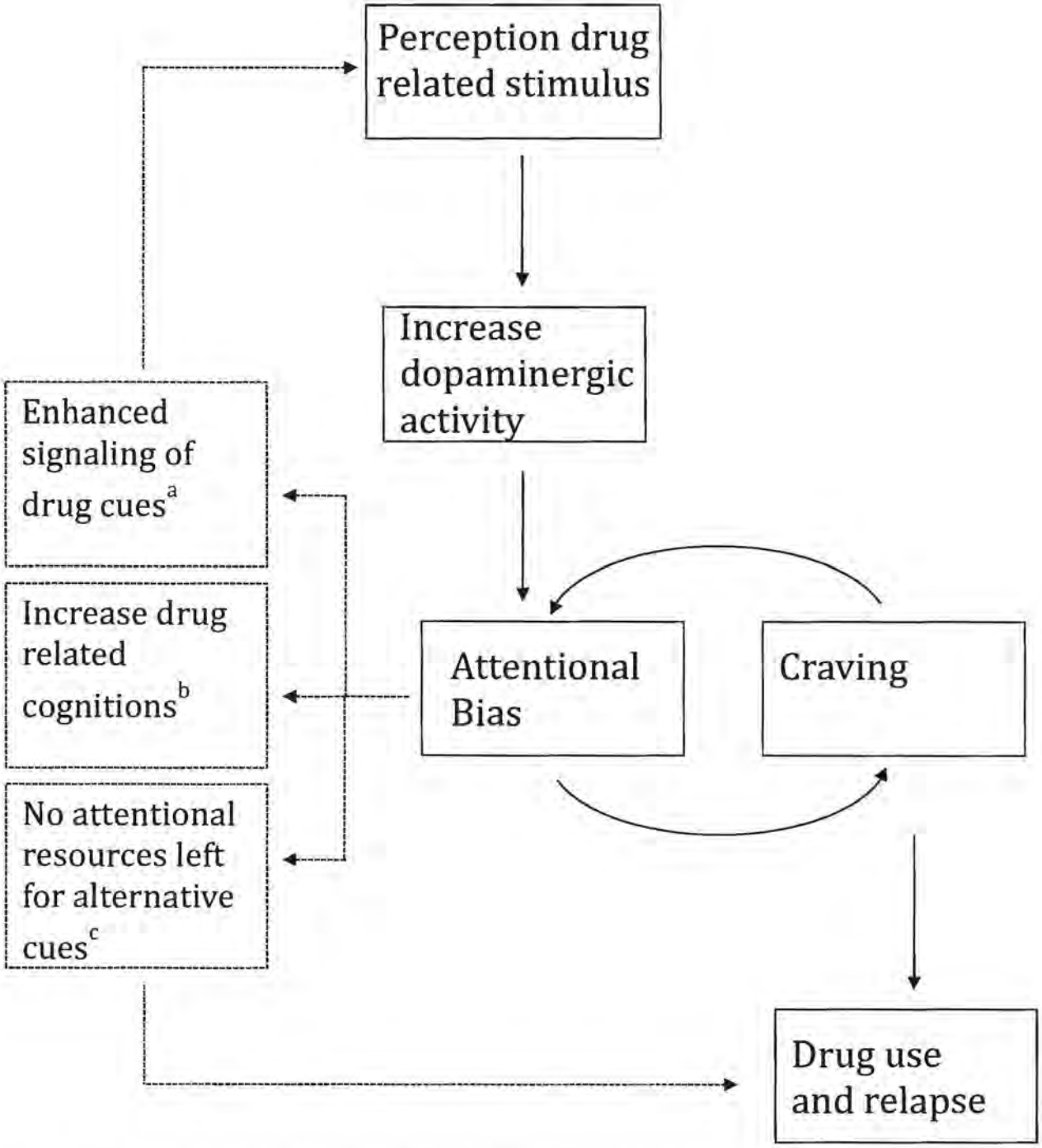


Figure 1: Reproduction of model by Franken (27) proposing the possible role of AB in craving and the combined effect on drug use and relapse.

Figure 1 Note:
[a]Further processing of the original cue or signaling of new cues.
[b]Memory bias, obsessive thoughts, preoccupation with drugs.
[c]e.g. control strategies, coping mechanisms.

Figure 2: Flow of participants in the study.

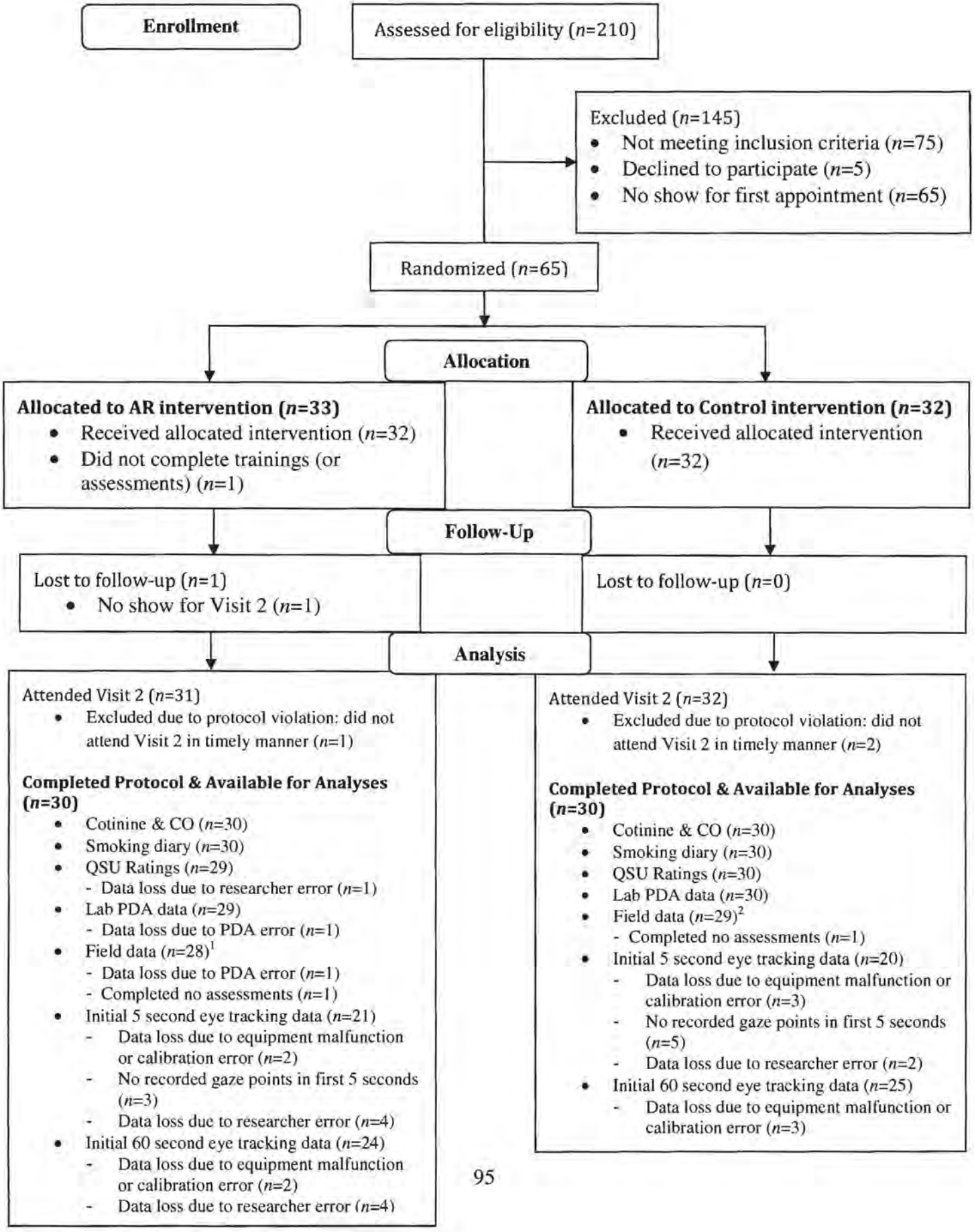

Enrollment
Assessed for eligibility (n=210)
Excluded (n=145)
• Not meeting inclusion criteria (n=75)
• Declined to participate (n=5)
• No show for first appointment (n=65)
Randomized (n=65)
Allocation
Allocated to AR intervention (n=33)
• Received allocated intervention (n=32)
• Did not complete trainings (or assessments) (n=1)
Allocated to Control intervention (n=32)
• Received allocated intervention (n=32)
Follow-Up
Lost to follow-up (n=1)
• No show for Visit 2 (n=1)
Lost to follow-up (n=0)
Analysis
Attended Visit 2 (n=31)
• Excluded due to protocol violation: did not attend Visit 2 in timely manner (n=1)
Completed Protocol & Available for Analyses (n=30)
• Cotinine & CO (n=30)
• Smoking diary (n=30)
• QSU Ratings (n=29)
- Data loss due to researcher error (n=1)
• Lab PDA data (n=29)
- Data loss due to PDA error (n=1)
• Field data (n=28)[1]
- Data loss due to PDA error (n=1)
- Completed no assessments (n=1)
• Initial 5 second eye tracking data (n=21)
- Data loss due to equipment malfunction or calibration error (n=2)
- No recorded gaze points in first 5 seconds (n=3)
- Data loss due to researcher error (n=4)
• Initial 60 second eye tracking data (n=24)
- Data loss due to equipment malfunction or calibration error (n=2)
- Data loss due to researcher error (n=4)
Attended Visit 2 (n=32)
• Excluded due to protocol violation: did not attend Visit 2 in timely manner (n=2)
Completed Protocol & Available for Analyses (n=30)
• Cotinine & CO (n=30)
• Smoking diary (n=30)
• QSU Ratings (n=30)
• Lab PDA data (n=30)
• Field data (n=29)[2]
- Completed no assessments (n=1)
• Initial 5 second eye tracking data (n=20)
- Data loss due to equipment malfunction or calibration error (n=3)
- No recorded gaze points in first 5 seconds (n=5)
- Data loss due to researcher error (n=2)
• Initial 60 second eye tracking data (n=25)
- Data loss due to equipment malfunction or calibration error (n=3)

Figure 2 note: Study Flowchart. Participants were randomly assigned to treatment conditions, stratified by gender. Due to researcher error, 16 males and 14 females completed the control condition.

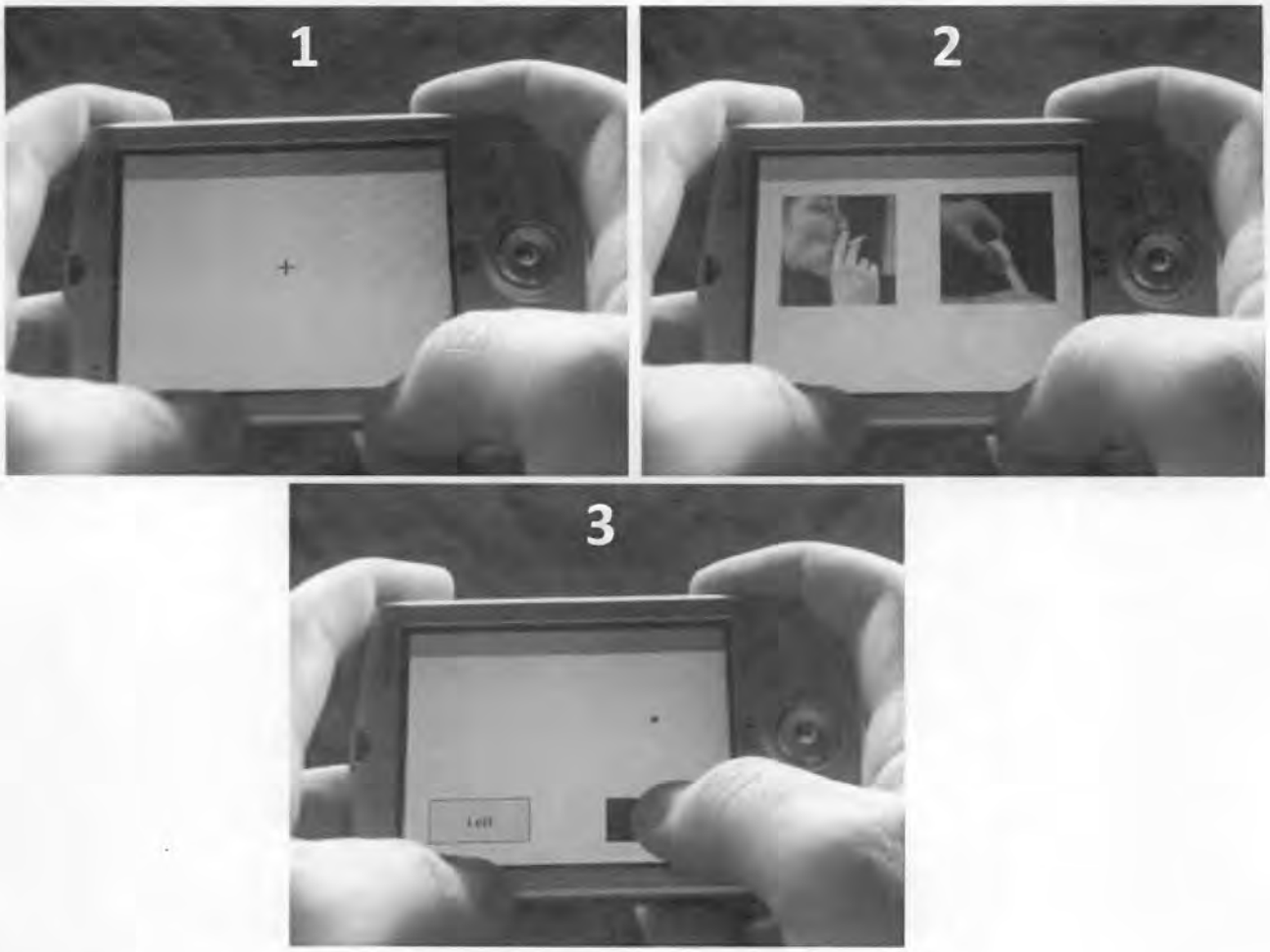


Figure 3: Screenshots of an individual completing the visual probe task.

Figure 3 Note: Figure and text adapted from Kerst (47). Diagram of sequence of events in a single VP trial. 1) The fixation cross is presented for 500ms, 2) the two pictures – one smoking and one neutral- are displayed (500 ms), and 3) the probe to which the participant must respond is presented.

Figure 4: Sample smoking stimulus used for cue-provoked items.

Figure 4 Note: Figure and text adapted from Kerst (47).

Figure 5: Video frames from the mobile-eye task for one example participant with lookzone, time stamp, and gaze fixations evident.

Figure 5 Note: Figure and text adapted from Kerst (47). Screenshot of five video frames over 5.00 second duration of mobile eye tracking for one participant. Gaze tracking indicated by red circle and crosshairs. lookzone (smoking stimuli) highlighted in yellow. Elapsed time out of 5.00 seconds presented in lower left-hand corner of each frame along with fixation duration (in parentheses) in seconds. Each frame reflects one fixation in order of occurrence. This participant had five fixations (the 'Total number of fixations' variable). One fixation occurred before fixating on the smoking stimuli (fixation 1). Two fixations were on the smoking stimuli (fixations 2 and 4; the 'Total number of fixations in smoking stimuli zone' variable). And three fixations were not on smoking stimuli (fixations 1, 3, and 5). Time not accounted for within fixations were either saccades, loss of pupil data required for eye tracking, or brief fixations lasting less than .200 seconds. Some of this additional time was spent looking at the smoking stimuli (reflected in the 'Total tracked time in smoking stimuli' and 'Total Gazepoints in smoking stimuli zone' variables).

Figure 6: Diagrammatic representation of the process used to arrive at 8 sets of 10 image pairs for use on the 8 days of participant training.

Step 1 Original set of 80 images

20 Human Smoking Images

20 Human Non-Smoking Images

20 No Human Smoking Images

20 No Human Non-Smoking Images

Step 2 2 sets of 20 image pairs

20 Human Smoking – Human Non-Smoking Image Pairs

20 No Human Smoking- No Human Non-Smoking Image Pairs

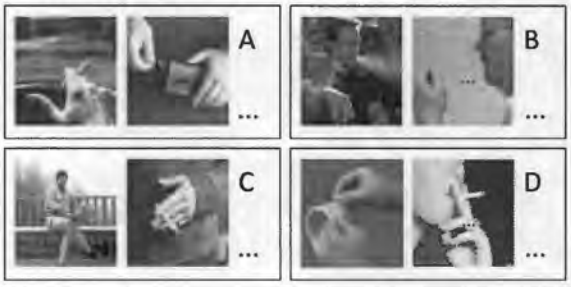
Step 3 2 more sets of 20 image pairs

20 Human Smoking – Human Non-Smoking Image Pairs

20 No Human Smoking- No Human Non-Smoking Image Pairs

Step 4 4 sets of 20 images pairs split Into 8 sets of 10 image pairs

4 sets of 10 Human Smoking – Human Non-Smoking Image Pairs



4 sets of 10 No Human Smoking- No Human Non-Smoking Image Pairs

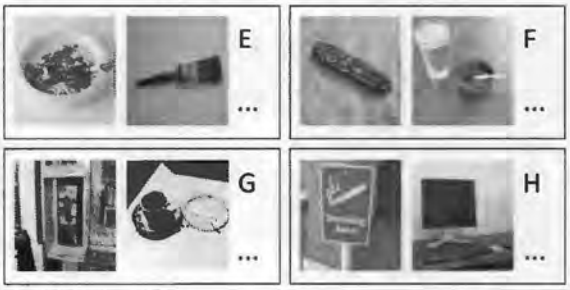


Figure 6 Note: Figure and text adapted from Kerst (47). **Step 1**: 80 individual images are selected from pool of hundreds, 20 images with humans and smoking stimuli, 20 with humans and no smoking stimuli, 20 without humans but with smoking stimuli, and 20 without humans and without smoking stimuli. **Step 2**: Smoking images are randomly paired with non-smoking images within the groups human and nonhuman for 2 sets of 20 image pairs. **Step 3**: The same 80 images are randomly paired in different pairs again for another 2 sets of 20 image pairs (same images, novel pairing). **Step 4**: The existing 4 sets of 20 image pairs are each split in half for 8 sets of 10 image pairs. These 8 sets are labeled A through H.

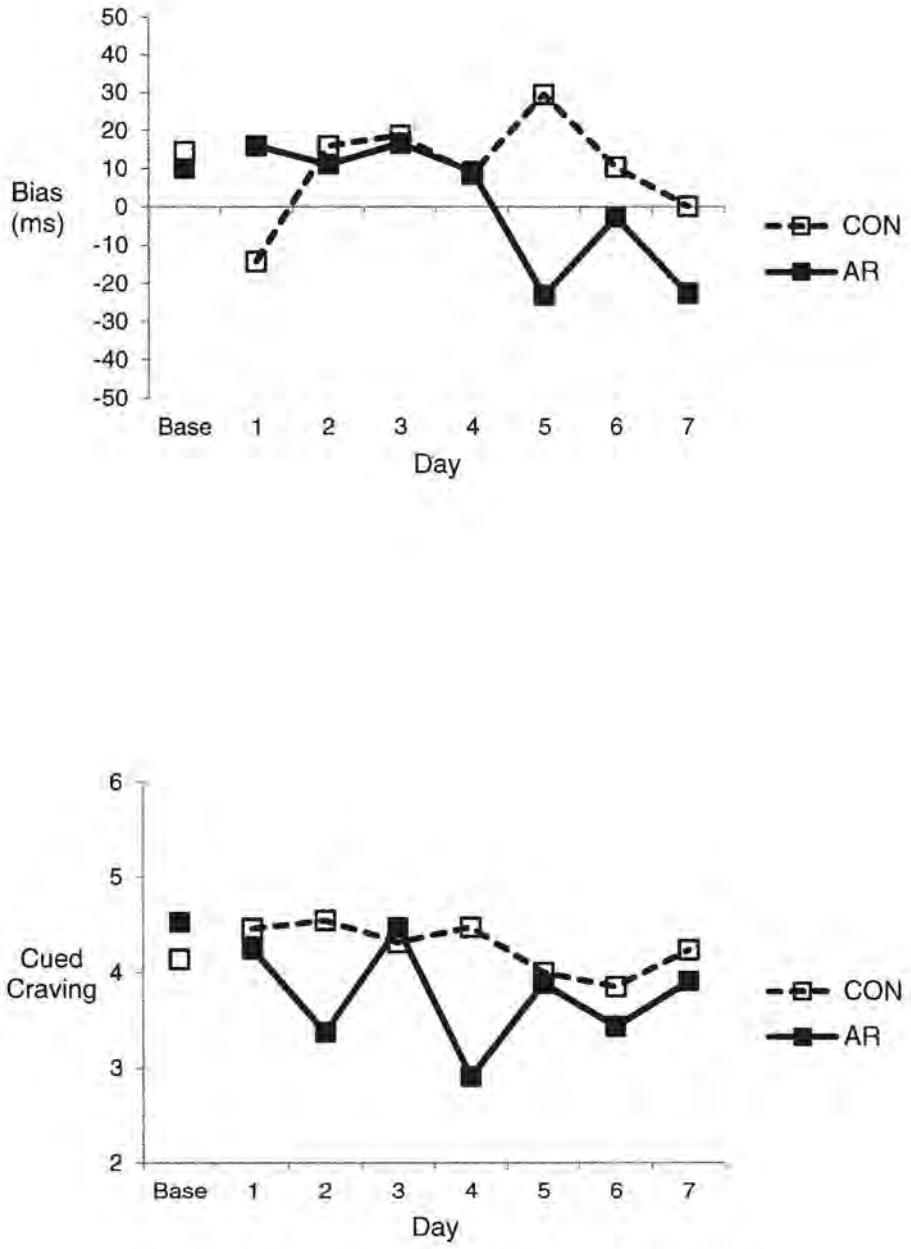


Figure 7: Effect of Training Group on attentional bias (upper graph) and cued craving (lower graph). AR = Attentional retraining group; CON =Control group; Base = baseline (pre-intervention)

DEMOGRAPHICS QUESTIONNAIRE

Q1. What is your date of birth? __ __ / __ __ / __ __ __ __

Refuse to Answer

Q2. What is your gender?

1 Male
2 Female

Q3. What is your present marital status? (Choose one)

1 Single
2 Married
3 Divorced
4 Widowed
5 Living with significant other
6 Separated
8 Refuse to Answer

Q4. How many years of education have you completed? (Choose one)

01 1 (Elementary School)
02 2 (Elementary School)
03 3 (Elementary School)
04 4 (Elementary School)
05 5 (Elementary School)
06 6 (Middle School)
07 7 (Middle School)
08 8 (Middle School)
09 9 (High School)
10 10 (High School)
11 11 (High School)
12 12 (High School)
13 13 (Some College)
14 14 (Vocational or Community College Degree)
16 16 (Four Year College Degree)
17 17 (Some Postgraduate Work)
18 18 (Postgraduate Degree; Master Degree)
20 20 (Postgraduate Degree; M.D., Ph.D., DDS, Dr.P.H., etc.)
98 Refuse to Answer

Q5. Are you of Hispanic/Latino origin?

1 Yes
0 No
8 Refuse to Answer

Q6. What category best describes your race? (Choose one)

1	Anglo American/Euro American/White
2	African American/Black
3	Asian American
4	Native of Hawaii or other Pacific Islander
5	Native American or Alaska Native
6	Mixed Race
7	Other
8	Refuse to Answer

If Q6 is equal to 8 or Q6 is less than 7, then skip to Q8.

Q7. Please specify your race_ __ __ __ __ __ __

Q8. Do you receive Medicare, Medicaid, or Medical Assistance currently?

1	Yes
0	No
7	Don't Know
8	Refuse to Answer

Q9. Do you have private insurance or group insurance?

1	Yes
0	No
7	Don't Know
8	Refuse to Answer

Q10. What is your total family income per year, before taxes? (Choose one)

01	Less than $10,000 per year or less than about $833 per month
02	$10,000 to $19,999 per year or less than about $1250 per month
03	$20,000 to $29,999 per year or less than about $2083 per month
04	$30,000 to $39,999 per year or less than about $2916 per month
05	$40,000 to $49,999 per year or less than about $3750 per month
06	$50,000 to $59,999 per year or less than about $4583 per month
07	$60,000 to $69,999 per year or less than about $5416 per month
08	$70,000 to $79,999 per year or less than about $6250 per month
09	$80,000 to $89,999 per year or less than about $7083 per month
10	$90,000 to $99,999 per year or less than about $7916 per month
11	$100,000 or more per year or more than $8333 per month
98	Refuse to Answer

Q11. Generations in the U.S. Please choose the best response: (Choose one)

1	I'm an immigrant of the US
2	I was born in the US
3	One of my parents and I were born in the US (the other parent immigrated)
4	My parents and I were born in the US
5	My grandparents, my parents, and I were born in the US
6	My great-grandparents and ancestors were born in the US
8	Refuse to Answer

If Q11 is greater than 1, then skip to Q13.

Q12. What year did you immigrate to the US? ____

Refuse to Answer

Q13. Employment Status. Please choose the best response: (Choose one)

01	Regular full-time (30 or more hours per week)
02	Regular part-time (less than 30 hours per week)
03	Unemployed, currently *looking* for work
04	Unemployed, currently *NOT looking* for work
05	Homemaker
06	Student
07	Retired
08	Unable to work or disabled
09	Other
98	Refuse to Answer

If Q13 is less than 9, then skip to Q15.

Q14. Please specify your employment status.

Q15. In the past 30 days, what was the primary source of your income? (Choose one)

1	A job
2	Unemployment Benefits
3	VA/Disability/Social Security Income
4	Welfare/Food Stamps/Aid to Family with Dependent Children
5	Alimony or Child Support
6	Spouse/partner is main source of income
8	Refuse to Answer

SMOKING HISTORY QUESTIONNAIRE

About how old were you when you first started smoking at least 1 cigarette a day? _____ **years old**

About how old were you when you started smoking regularly **everyday**? _____ **cigarettes a day**

How many cigarettes do you smoke on a **normal day**? _____ **cigarettes a day**

	Definitely not	**Probably not**	**Possibly**	**Probably**	**Definitely**
Do you think you are addicted to smoking?	☐	☐	☐	☐	☐

Are you seriously thinking of quitting smoking?

☐ Yes, within the next 30 days

☐ Yes, within the next 6 months

☐ No, not thinking of quitting

	Yes	**No**
Have you used any other tobacco products (i.e., cigars, pipes, smokeless tobacco, bidis, cloves)?	☐	☐

Describe:

	Yes	**No**
Have you ever made a serious and deliberate attempt to **STOP SMOKING** cigarettes completely?	☐	☐

If so, how many times? _____ times

In the **last year**, how many times have you quit smoking for at least 24 hours? _____ times

How hard was it for you to quit smoking on your most recent attempt?

Easy	Slightly Difficult	Difficult	Very Difficult

How severely did you experience any of the following symptoms below in your most recent attempt to quit smoking? Choose the answer that most reflects the severity of each symptom.

	Not at all	Mild	Moderate	Severe	Very severe
Cravings for cigarettes	1	2	3	4	5
Irritability	1	2	3	4	5
Nervousness	1	2	3	4	5
Difficulty concentrating	1	2	3	4	5
Physical symptoms	1	2	3	4	5
Difficulty sleeping	1	2	3	4	5

FTND

	Within 5 minutes	6 to 30 minutes	31 to 60 minutes	After 60 minutes
How soon after you wake up do you smoke your **first** cigarette?	☐	☐	☐	☐

	Yes	No
Do you find it difficult to refrain from smoking in places where it is forbidden, e.g., in church, at the library, in the cinema, etc.?	☐	☐

	The first cigarette in the morning	Any cigarette other than the first one
Which cigarette would you hate to give up most?	☐	☐

	10 or less	11-20	21-30	31 or more
How many cigarettes per day do you smoke?	☐	☐	☐	☐

	Yes	No
Do you smoke more frequently during the first hours after waking than the rest of the day?	☐	☐

	Yes	No
Do you smoke if you are so ill that you are in bed most of the day?	☐	☐

QUESTIONNAIRE FOR SMOKING URGES

Instructions: Indicate how much you agree or disagree with each of the following statements by circling the number between strongly disagree and strongly agree. The closer you choose a number to one end or the other indicates the strength of your disagreement or agreement. Please complete every item. We are interested in how you are thinking or feeling **right now** as you are filling out the questionnaire.

	Strongly Disagree					**Strongly Agree**
1. I have a desire for a cigarette.	0	1	2	3	4	5
2. Nothing would be better than smoking a cigarette.	0	1	2	3	4	5
3. If it were possible, I probably would smoke a cigarette.	0	1	2	3	4	5
4. I would control things better if I could smoke.	0	1	2	3	4	5
5. All I want is a cigarette.	0	1	2	3	4	5
6. I have an urge for a cigarette.	0	1	2	3	4	5
7. A cigarette would taste good.	0	1	2	3	4	5
8. I would do almost anything for a cigarette.	0	1	2	3	4	5
9. Smoking would make me less depressed.	0	1	2	3	4	5
10. I am going to smoke as soon as possible.	0	1	2	3	4	5

BIDR Version 6 – Form 40

Using the scale below as a guide, write a number beside each statement to indicate how much you agree with it.

1----------2----------3----------4----------5----------6----------7
NOT TRUE SOMEWHAT TRUE VERY TRUE

_____ 1. My first impressions of people usually turn out to be right.
_____ 2. It would be hard for me to break any of my bad habits.
_____ 3. I don't care to know what other people really think of me.
_____ 4. I have not always been honest with myself.
_____ 5. I always know why I like things.
_____ 6. When my emotions are aroused, it biases my thinking.
_____ 7. Once I've made up my mind, other people can seldom change my opinion.
_____ 8. I am not a safe driver when I exceed the speed limit.
_____ 9. I am fully in control of my own fate.
_____ 10. It's hard for me to shut off a disturbing thought.
_____ 11. I never regret my decisions.
_____ 12. I sometimes lose out on things because I can't make up my mind soon enough.
_____ 13. The reason I vote is because my vote can make a difference.
_____ 14. My parents were not always fair when they punished me.
_____ 15. I am a completely rational person.
_____ 16. I rarely appreciate criticism.
_____ 17. I am very confident of my judgments.
_____ 18. I have sometimes doubted my ability as a lover.
_____ 19. It's all right with me if some people happen to dislike me.
_____ 20. I don't always know the reasons why I do the things I do.
_____ 21. I sometimes tell lies if I have to.
_____ 22. I never cover up my mistakes.
_____ 23. There have been occasions when I have taken advantage of someone.
_____ 24. I never swear.
_____ 25. I sometimes try to get even rather than forgive and forget.
_____ 26. I always obey laws, even if I'm unlikely to get caught.
_____ 27. I have said something bad about a friend behind his or her back.
_____ 28. When I hear people talking privately, I avoid listening.
_____ 29. I have received too much change from a salesperson without telling him or her.
_____ 30. I always declare everything at customs.
_____ 31. When I was young I sometimes stole things.
_____ 32. I have never dropped litter on the street.
_____ 33. I sometimes drive faster than the speed limit.
_____ 34. I never read sexy books or magazines.
_____ 35. I have done things that I don't tell other people about.
_____ 36. I never take things that don't belong to me.
_____ 37. I have taken sick-leave from work or school even though I wasn't really sick.
_____ 38. I have never damaged a library book or store merchandise without reporting it.

_____ 39. I have some pretty awful habits.
_____ 40. I don't gossip about other people's business.

UNIFORMED SERVICES UNIVERSITY
BETHESDA, MARYLAND

This consent form is valid only if it contains the IRB stamped date

Consent for Voluntary Participation in a Non-Clinical Research Study

1. INTRODUCTION OF THE STUDY

You are being asked to be in a research study entitled "Attention Training in Smokers" at the Uniformed Services University of the Health Sciences (USUHS), Bethesda, Maryland. You have been asked to take part in this study because you are a smoker. Your participation is voluntary. Refusal to participate will not result in any punishment or loss of benefits to which you are otherwise permitted. Please read the information below, and ask questions about anything you do not understand, before deciding whether to take part in the study.

2. PURPOSE OF THE STUDY

The purpose of this behavioral research study is to evaluate a new method of influencing smokers' attention, cravings and smoking. Results from this study may help researchers create more effective cessation (quitting) programs in the future. If you agree to be part of the study, you will be randomly assigned to one of two training conditions. You will not know which condition you are in. This is the normal procedure in this type of study. In previous research by other investigators, the attention training has been delivered on a desktop computer in a laboratory setting. This research has shown that these two conditions can influence smokers' attention, cravings, and smoking differently. In this study, we want to see if we can deliver the training effectively on a PDA (a hand-held computer).

3. PROCEDURES TO BE FOLLOWED

You will attend up to 2 laboratory sessions in Building 28 at USUHS. The first laboratory session will last about 90 minutes and the second laboratory session will last about 60 minutes. You will first attend an orientation session. If you are eligible and you agree to be in this study, a research staff member will show you how to use the PDA. You will complete an assessment on the PDA. You will be asked to complete some brief questionnaires assessing your demographics (such as your age and income), your smoking, and your personality. You will be given a smoking diary and asked to record the number of cigarettes you smoke each day for the next week. You can smoke as much or as little as you like during the week.

You will be asked to carry a PDA around with you for 1 week. The PDA will beep you at random times during the day (about 4 times each day). After the PDA beeps you, you will be asked to respond to a series of questions which ask you how you are feeling at that time. You will perform a reaction time task on the PDA. Each PDA assessment should last about 10 minutes in total.

At the end of the study, you will be asked to attend a second session at which you will return the PDA and the smoking diary. You will complete an assessment on the PDA. You will also perform a brief task in which we will measure where you look using a device that measures eye positions. For this task, you will wear a spectacle with a mini camera, and a light recording device on a hip-pack, for a brief duration.

At both the orientation and second sessions, you will be asked to provide a breath sample and a saliva sample. The breath sample and the saliva sample will help the researchers find out how much you have smoked. At the orientation session, the level of carbon monoxide in your breath must be above a certain level in order for you to be eligible for the study. Your craving for cigarettes will also be assessed.

When your participation in the study is over, you will be offered self-help materials for quitting smoking and a referral to smoking cessation programs.

4. NUMBER OF PEOPLE THAT WILL TAKE PART IN THIS STUDY

Up to 96 individuals are expected to participate in this study.

5. AMOUNT OF TIME FOR YOU TO COMPLETE THE STUDY

Participation of this study will require in total about 6 and a half hours of your time over a period of about 1 week.

6. ELIGIBILITY AND PAYMENT FOR BEING IN THIS STUDY

Participation:

Civilians and military personnel may participate in this study. Federal civilians and military personnel must provide the investigators with a signed Statement of Approval form.

Compensation:

Civilians may receive compensation for their participation in this study. Military personnel cannot receive compensation for their participation.

Non-federal civilians will receive $20 for completing the orientation session (even

if ineligible), and $20 for completing the second laboratory session. Non-federal civilians will receive $2 for each PDA assessment that they complete. They will also receive $5 for each day (except the final day) that they contribute data to the study, up to a maximum of 7 days. If a non-federal civilian completes all scheduled PDA assessments, they will receive approximately $131 ($20 (orientation session) + $35 (days completed in study) + $20 (second laboratory session) + ($2 x 28) (PDA assessments)).

Federal civilians will only receive compensation for the laboratory sessions and the PDA assessments that occur during non-duty hours. For example, if a federal civilian completes the orientation and second laboratory session during non-duty hours, and completes 1 PDA assessment per day during non-duty hours, they will receive $89 ($20 (orientation session) + $35 (days completed in study) + $20 (second laboratory session) + ($2 x 7) (PDA assessments)).

A check will be mailed to civilians following completion of the study.

7. POSSIBLE RISKS OR DISCOMFORTS FROM BEING IN THIS STUDY

The risks or discomforts from being in this study are expected to be minimal. There are no known risks associated with completing the laboratory assessments or the PDA assessments. There is no reason to believe that your smoking will be increased by participation in the study.

You may refuse to answer any question that makes you feel uncomfortable. If you have concerns after completing the questionnaires, you are encouraged to contact your doctor or the study chair.

If something in this research makes you uncomfortable or upset, you may choose to stop taking part in this research at any time without loss of benefits; you may contact the investigator for referral. If the investigators note any distress or anxiety associated with the research, you will receive referrals, if appropriate.

8. POSSIBLE BENEFITS FROM BEING IN THIS STUDY

Some participants may reduce their smoking over the course of the week. Some participants may experience reduced cravings. However, no benefit can be guaranteed.

The information we learn may help us develop better smoking cessation programs. Therefore, smokers may benefit from what is learned. This may be beneficial to society.

9. CONFIDENTIALITY/PRIVACY AND HOW YOUR IDENTITY AND YOUR RESEARCH RECORDS WILL BE MAINTAINED

All information you provide as part of this study will be confidential and will be protected to the fullest extent provided by law. Your responses to our laboratory

and PDA assessments will be maintained in a locked filing cabinet or on a password-protected computer in lab offices in the Department of Medical and Clinical Psychology. All records related to this study will be accessible to those persons directly involved in conducting this study and members of the USUHS Institutional Review Board (IRB), which provide oversight for protection of human research volunteers. In addition, the IRB at USUHS and other federal agencies that help protect people who are involved in research studies, may need to see the information you give us. Other than those groups, records from this study will be kept private to the fullest extent of the law. Scientific reports that come out of this study will not use your name or identify you in any way.

The breath sample you provide will allow us to measure carbon monoxide (CO) levels in your breath. This will allow us to measure how much you have smoked. We will use a standard CO monitor (Vitalograph, Lexena, KS) according to the manufacturer's instructions. Data on your CO levels will be stored on a password-protected EXCEL spreadsheet on a computer in Room 113 of Building 28. The password is only known to the research staff.

To prepare for the saliva sample, you will be asked to refrain from eating and drinking for 10 minutes before sampling. You will be offered a moist towelette to clean/wipe your hands/mouth. Using gloves, the research assistant will open the vial and give you the cotton roll. You will be asked to place the cotton piece in your mouth and to gently roll it in your mouth for a whole minute to saturate with saliva. You are requested to place most of the cotton piece on the edge of your mouth and re-insert it to the vial without touching the vial. Using gloves, the research assistant will tightly replace the cap on the vial.

The saliva samples will be stored in a freezer (-80F) in Building 28 for up to three months. Batches of saliva samples will be sent to Salimetrics, Inc. (www.salimetrics.com). Salimetrics, LLC, will perform an assay (a test) on each sample to determine the level of cotinine in the saliva. Cotinine is a breakdown product of nicotine and tells us how much your smoked during the past few days. No other tests will be performed on the saliva samples.

Only the study researchers will have access to the saliva samples. The samples are labeled with the participant study number (and visit number); only the research staff know the linkages between study numbers and participants. Thus, confidentiality is maintained during storage and distribution. The shipping procedures follow the U.S. Centers for Disease Control (CDC) guidelines for transport of biological specimens. Once the cotinine assay is performed, Salimetrics, LLC will destroy the samples. Because you are free to drop out of the study at any time, you can request that your saliva samples are destroyed. Saliva samples will only be stored at USUHS.

10. CONDITIONS WHICH YOUR PARTICIPATION IN THIS STUDY MAY BE STOPPED WITHOUT YOUR CONSENT

The investigator may stop you from taking part in this study if being in the study is unsafe or dangerous to you or if you lose your right to receive medical care at military hospitals. The investigator may also stop you participating if you experience difficulty in following the procedures.

11. IF YOU DECIDE TO STOP TAKING PART IN THIS STUDY AND THE INSTRUCTIONS FOR STOPPING EARLY

You have the right to withdraw from this study at any time. If you decide to stop taking part in this study, you should tell the principal investigator as soon as possible; by leaving this study at any time, you in no way risk losing your right to medical care.

12. RECOURSE IN THE EVENT OF INJURY

If at any time you believe you have suffered an injury or illness as a result of participating in this research project, you should contact the Director of Human Research Protections Programs at the Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814-4799 at (301) 295-9534. This office can review the matter with you, can provide information about your rights as a subject, and may be able to identify resources available to you. If you believe the government or one of the government's employees (such as a military doctor) has injured you, a claim for damages (money) against the federal government (including the military) may be filed under the Federal Torts Claims Act. Information about judicial avenues of compensation is available from the University's General Counsel at (301) 295-3028.

CONTACT FOR QUESTIONS OR PROBLEMS

If you have questions about this research, you should contact William Kerst, the person in charge of the study. William's number at USUHS is 301 295-1520. Even in the evening or on weekends, you can leave a message at that number. If you have questions about your rights as a research subject, you should call the Director of Human Research Protections Programs at USUHS at (301) 295-9534. She is your representative and has no connection to the researcher conducting this study.

SIGNATURE OF RESEARCH PARTICIPANT OR LEGAL REPRESENTATIVE

You have read (or someone has read to you) the information in this consent form. You have been given a chance to ask questions and all of your questions have been answered to your satisfaction.

BY SIGNING THIS CONSENT FORM, YOU FREELY AGREE TO TAKE PART IN THE RESEARCH IT DESCRIBES.

Participant's Signature Date

Participant's Printed Name

SIGNATURE OF INVESTIGATOR/RESEARCH TEAM MEMBER

You have explained the research to the participant, or his/her legal representative, and answered all of his/her questions. You believe that the volunteer subject understands the information described in this document and freely consents to participate.

Investigator's/Research Team Member's Signature Date (must be the same as the participant's)

Investigator's/ Research Team Member's Printed Name

SIGNATURE OF WITNESS

Your signature as witness is intended to attest that the information in the consent document and any other information was explained to and apparently understood by the participant, or the participant's legal representative, that questions and concerns were addressed and that informed consent was freely given.

Witness' Signature Date (must be the same as the participant's)

Witness' Printed Name

REFERENCES

1. Ali-Hasan N, Harrington E, & Richman J. 2008. *Best practices for eye tracking of television and video user experiences.* Presented at the 1st international conference on Designing interactive user experiences for TV and video, Silicon Valley, California, USA

2. Attwood AS, O'Sullivan H, Leonards U, Mackintosh B, & Munafo MR. 2008. Attentional bias training and cue reactivity in cigarette smokers. *Addiction*, 103(11): 1875

3. Beard C, Sawyer AT, & Hofmann SG. 2012. Efficacy of attention bias modification using threat and appetitive stimuli: a meta-analytic review. *Behavior Therapy*, 43(4): 724-740

4. Behar E, McHugh RK, Peckham A, & Otto MW. 2010. D-cycloserine for the augmentation of an attentional training intervention for trait anxiety. *Journal of anxiety disorders*, 24(4): 440-445

5. Berridge KC. 2009. Wanting and liking: observations from the neuroscience and psychology laboratory. *Inquiry*, 52(4): 378-398

6. Bradley B, Garner M, Hudson L, & Mogg K. 2007. Influence of negative affect on selective attention to smoking-related cues and urge to smoke in cigarette smokers. *Behavioural Pharmacology*, 18(4): 255

7. Browning M, Holmes EA, Murphy SE, Goodwin GM, & Harmer CJ. 2010. Lateral prefrontal cortex mediates the cognitive modification of attentional bias. *Biological Psychiatry*, 67(10): 919-925

8. Carpenter KM, Schreiber E, Church S, & McDowell D. 2006. Drug Stroop performance: Relationships with primary substance of use and treatment outcome in a drug-dependent outpatient sample. *Addictive Behaviors*, 31(1): 174-181

9. Centers for Disease Control and Prevention. 2012. *Cigarette smoking among adults – United States, 2011.* CDC Morbidity and Mortality Weekly Report, 61(44): 889-894

10. Cohen S, Lichtenstein E, Prochaska JO, Rossi JS, Gritz ER, Carr CR, ... & Ossip-Klein D. 1989. Debunking myths about self-quitting: Evidence from 10 prospective studies of persons who attempt to quit smoking by themselves. *American Psychologist*, 44(11): 1355

11. Cooper MJ, Anastasiades P, & Fairburn CG. 1992. Selective processing of eating-, shape-, and weight-related words in persons with bulimia nervosa. *Journal of Abnormal Psychology*, 101(2): 352-355

12. Cox WM, Fadardi JS, & Pothos EM. 2006. The addiction-Stroop test: Theoretical considerations and procedural recommendations. *Psychological Bulletin*, 132(3): 443

13. Cox WM, Hogan LM, Kristian MR, & Race JH. 2002. Alcohol attentional bias as a predictor of alcohol abusers' treatment outcome. *Drug and Alcohol Dependence*, 68(3): 237-243

14. Cox LS, Tiffany ST, & Christen AG. 2001. Evaluation of the brief questionnaire of smoking urges (QSU-brief) in laboratory and clinical settings. *Nicotine and Tobacco Research*, 3(1): 7-16

15. Dean AC, Sevak RJ, Monterosso JR, Hellemann G, Sugar CA, & London ED. 2011. Acute modafinil effects on attention and inhibitory control in methamphetamine-dependent humans. *Journal of Studies on Alcohol and Drugs*, 72(6): 943

16. Donovan J, & Radosevich D. 1999. A meta-analytic review of the distribution of practice effect: Now you see it, now you don't. *Journal of Applied Psychology*, 84: 795-805

17. Evans KM, Jacobs RA, Tarduno JA, & Pelz JB. 2012. Collecting and analyzing eye-tracking data in outdoor environments. *Journal of Eye Movement Research*, 5(2): 1-19

18. Fadardi JS, & Cox WM. 2009. Reversing the sequence: Reducing alcohol consumption by overcoming alcohol attentional bias. *Drug and Alcohol Dependence*, 101(3): 137-145

19. Field M, & Cox WM. 2008. Attentional bias in addictive behaviors: A review of its development, causes, and consequences. *Drug and Alcohol Dependence*, 97(1): 1-20

20. Field M, Duka T, Tyler E, & Schoenmakers T. 2009. Attentional bias modification in tobacco smokers. Nicotine and Tobacco Research, 11(7): 812-822.

21. Field M, & Eastwood B. 2005. Experimental manipulation of attentional bias increases the motivation to drink alcohol. *Psychopharmacology*, 183(3): 350-357

22. Field M, Duka T, Eastwood B, Child R, Santarcangelo M, & Gayton M. 2007. Experimental manipulation of attentional biases in heavy drinkers: Do the effects generalise?. *Psychopharmacology*, 192(4): 593-608

23. Field M, Mogg K, & Bradley B. 2004. Eye-movements to smoking related cues: Effects of nicotine deprivation. *Psychopharmacology*, 173: 116-123

24. Field M, Munafò MR, & Franken IH. 2009. A meta-analytic investigation of the relationship between attentional bias and subjective craving in substance abuse. *Psychological Bulletin*, 135(4): 589

25. Findlay J, & Gilchrist I. 2003. *Active vision: The psychology of looking and seeing*. Oxford: Oxford University Press

26. Fox E, Russo R, & Dutton K. 2002. Attentional bias for threat: Evidence for delayed disengagement from emotional faces. *Cognition & Emotion*, 16(3): 355-379

27. Franken IHA. 2003. Drug craving and addiction: Integrating psychological and neuropsychopharmacological approaches. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 27(4): 563-579

28. Franken I, Kroon L, & Hendriks V. (2000a). Influence of individual differences in craving and obsessive cocaine thoughts on attentional processes in cocaine abuse patients. *Addictive Behaviors*, 25(1): 99-102

29. Franken I, Kroon L, Wiers R, & Jansen A. 2000b. Selective cognitive processing of drug cues in heroin dependence. *Journal of Psychopharmacology*, 14(4): 395

30. Garvey AJ, Bliss RE, Hitchcock JL, Heinold JW, & Rosner B. 1992. Predictors of smoking relapse among self-quitters: A report from the normative aging study. *Addictive Behaviors*, 17(4): 367-377

31. Gilbert D, Sugai C, Zuo Y, Rabinovich N, McClernon F, & Froeliger B. 2007. Brain indices of nicotine's effects on attentional bias to smoking and emotional pictures and to task-relevant targets. *Nicotine & Tobacco Research*, 9(3): 351

32. Hallion LS, & Ruscio AM. 2011. A meta-analysis of the effect of cognitive bias modification on anxiety and depression. *Psychological Bulletin*, 137(6): 940

33. Hakamata Y, Lissek S, Bar-Haim Y, Britton JC, Fox NA, Leibenluft E, ... & Pine DS. 2010. Attention bias modification treatment: a meta-analysis toward the establishment of novel treatment for anxiety. *Biological Psychiatry*, 68(11): 982-990

34. Hazen RA, Vasey MW, & Schmidt NB. 2009. Attentional retraining: A randomized clinical trial for pathological worry. *Journal of Psychiatric Research*, 43(6): 627-633

35. Heatherton TF, Kozlowski LT, Frecker RC, & Fagerstrom KO. 1991. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. *Addiction*, 86(9): 1119-1127

36. Henderson J. 2006. Eye movements. In *Methods in Mind*, ed. C. Senior, T. Russell & M. Gazzaniga. pp. 171-191. Cambridge, MA: The MIT Press

37. Hofmann W, Friese M, & Wiers R. 2008. Impulsive versus reflective influences on health behavior: A theoretical framework and empirical review. *Health Psychology Review*, 2(2): 111-137

38. Hogarth L, Dickinson A, Hutton S, Elbers N, & Duka T. 2006. Drug expectancy is necessary for stimulus control of human attention, instrumental drug-seeking behaviour and subjective pleasure. *Psychopharmacology*, 185(4): 495-504

39. Hogarth L, Dickinson A, Janowski M, Nikitina A, & Duka T. 2008. The role of attentional bias in mediating human drug-seeking behaviour. *Psychopharmacology*, 201(1): 29-41

40. Hoppitt L, Mathews A, Yiend J, & Mackintosh B. 2010. Cognitive bias modification: The critical role of active training in modifying emotional responses. *Behavior Therapy*, 41(1): 73-81

41. Hughes JR, Gulliver SB, Fenwick JW, Valliere WA, Cruser K, Pepper S, ... & Flynn BS. 1992. Smoking cessation among self-quitters. *Health Psychology*, 11(5): 331

42. Hughes JR, Higgins ST, & Hatsukami D. 1990. Effects of abstinence from tobacco (a critical review). *Research Advances in Alcohol & Drug Problems*, 10: 317-398

43. Janes AC, Pizzagalli SR, Richardt S, Frederick BD, Chuzi S, Pachas G, Culhane MA,...Kaufman MJ. 2010. Brain reactivity to smoking cues prior to smoking cessation predicts ability to maintain tobacco abstinence. *Biological Psychiatry*, 67: 722-729

44. Jarvik ME. 1970. The role of nicotine in the smoking habit. *Learning mechanisms in smoking*: 155-190

45. Jorenby DE, Leischow SJ, Nides MA, Rennard SI, Johnston JA, Hughes AR, ... & Baker TB. 1999. A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. *New England Journal of Medicine*, 340(9): 685-691

46. Kato, S., Boon, C. S., Fujibayashi, A., Hangai, S., & Hamamoto, T. (2005) Perceptual quality of motion of video sequences on mobile terminals. *Proceedings 2005 Signal and Image Processing*, Honolulu, HI, August 15-17, pp. 442-447

47. Kerst W. 2011. *Attention training in smokers: A feasibility study of an ecological momentary assessment approach.* (unpublished Master's thesis) Uniformed Services University of the Health Sciences, Bethesda, MD

48. Klingberg T, Forssberg H, & Westerberg H. 2002. Training of working memory in children with ADHD. *Journal of Clinical and Experimental Neuropsychology*, 24(6): 781-791

49. Kwak S, Na D, Kim G, Kim G, & Lee J. 2007. Use of eye movement to measure smokers' attentional bias to smoking-related cues. *Cyberpsychology and Behavior*, 10(2): 299-304

50. Lee CW, & Kahende J. 2007. Factors associated with successful smoking cessation in the United States, 2000. *American Journal of Public Health*, 97(8): 1503-1509

51. Lubman DI, Peters LA, Mogg K, Bradley BP, & Deakin JFW. 2000. Attentional bias for drug cues in opiate dependence. *Psychological Medicine*, 30(1): 169

52. Lynch B. 2002. Historical review of computer-assisted cognitive retraining. *The Journal of Head Trauma Rehabilitation*, 17(5): 446

53. MacKinnon DP. 2008. *Introduction to statistical mediation analysis*. New York: Taylor and Francis Group

54. MacLeod C, Mackintosh B, & Vujic T. 2009. *Does the explicit communication of the training contingency enhance the efficacy of cognitive behavior modification (CBM).* Paper presented at the special meeting on Cognitive Bias Modification in Emotional Disorders and Addiction: New developments. Ghent, Belgium.

55. MacLeod C, Mathews A, & Tata P. 1986. Attentional bias in emotional disorders. *Journal of Abnormal Psychology*, 95(1): 15-20

56. MacLeod C, Rutherford E, Campbell L, Ebsworthy G, & Holker L. 2002. Selective attention and emotional vulnerability: Assessing the causal basis of their association through the experimental manipulation of attentional bias. *Journal of Abnormal Psychology*, 111(1): 107-123

57. Marhe R, Waters AJ, van de Wetering BJ, & Franken IH. 2013. Implicit and explicit drug-related cognitions during detoxification treatment are associated with drug relapse: An ecological momentary assessment study. *Journal of Consulting and Clinical Psychology*, 81(1): 1

58. Marissen MA, Franken IH, Waters AJ, Blanken P, van den Brink W, & Hendriks VM. 2006. Attentional bias predicts heroin relapse following treatment. *Addiction*, 101(9): 1306-1312.

59. Mathews A, & Mackintosh B. 1998. A cognitive model of selective processing in anxiety. *Cognitive Therapy and Research*, 22(6): 539-560

60. Mathews A, & MacLeod C. 2002. Induced processing biases have causal effects on anxiety. *Cognition and Emotion*, 16(3): 331-354

61. McHugh RK, Murray HW, Hearon BA, Calkins AW, & Otto MW. 2010. Attentional bias and craving in smokers: the impact of a single attentional training session. *Nicotine & Tobacco Research*, 12(12): 1261-1264

62. McClernon FJ, & Choudhury RR. 2013. I am your smartphone and I know you are about to smoke: The application of mobile sensing and computing approaches to smoking research and treatment. *Nicotine & Tobacco Research*, (epub ahead of print).

63. Miller MA, & Fillmore MT. 2010. The effect of image complexity on attentional bias towards alcohol - related images in adult drinkers. *Addiction*, 105(5): 883-890

64. Mogg K, & Bradley BP. 1998. A cognitive-motivational analysis of anxiety. *Behaviour Research and Therapy*, 36(9): 809-848

65. Mogg K, Bradley B, Field M, & De Houwer J. 2003. Eye movements to smoking-related pictures in smokers: Relationship between attentional biases and implicit and explicit measures of stimulus valence. *Addiction*, 98: 825-836

66. Mogg K, Field M, & Bradley B. 2005. Attentional and approach biases for smoking cues in smokers: an investigation of competing theoretical views of addiction. *Psychopharmacology*, 180(2): 333-341

67. Norberg MM, Krystal JH, & Tolin DF. 2008. A meta-analysis of D-cycloserine and the facilitation of fear extinction and exposure therapy. *Biological Psychiatry*, 63(12): 1118-1126

68. Onur OA, Schlaepfer TE, Kukolja J, Bauer A, Jeung H, Patin A, ... & Hurlemann R. 2010. The N-methyl-D-aspartate receptor co-agonist D-cycloserine facilitates declarative learning and hippocampal activity in humans. *Biological Psychiatry*, 67(12): 1205

69. Ossip-Klein DJ, Bigelow G, Parker SR, Curry S, Hall S, & Kirkland S. 1986. Classification and assessment of smoking behavior. *Health Psychology*, 5: 3-11

70. Patten CA, & Martin JE. 1996. Does nicotine withdrawal affect smoking cessation? Clinical and theoretical issues. *Annals of Behavioral Medicine*, 18(3): 190-200

71. Paulhus DL. 2006. *Balanced Inventory of Desirable Responding (BIDR).* Acceptance and Commitment Therapy. Measures Package. 41

72. Petry NM. 2013. *Contingency management for substance abuse treatment: A guide to implementing this evidence-based practice.* New York: Routledge

73. Posner MI, Snyder CR, & Davidson BJ. 1980. Attention and the detection of signals. *Journal of Experimental Psychology*, 109(2): 160-174

74. Potenza MN, Sofuoglu M, Carroll KM, & Rounsaville BJ 2011. Neuroscience of behavioral and pharmacological treatments for addictions. *Neuron*, 69(4): 695-712

75. Ratcliff R. 1993. Methods for dealing with reaction time outliers. *Psychological Bulletin*, 114: 510-510

76. Razeghi R. 2010. *Usability of eye tracking as a user research technique in geo-information processing and dissemination.* (unpublished Master's thesis) International Institute of Geo-Information Science and Earth Observation, Enschede, Netherlands

77. Reber AS. 1967. Implicit learning of artificial grammars. *Journal of Verbal Learning and Verbal Behavior*, 6(6): 855-863

78. Reber AS. 1989. Implicit learning and tacit knowledge. *Journal of experimental psychology: General*, 118(3): 219

79. Robinson TE, & Berridge KC. 1993. The neural basis of drug craving: An incentive-sensitization theory of addiction. *Brain Research Reviews*, 18(3): 247-291

80. Rose AK, Brown K, Field M, & Hogarth L. 2013. The contributions of value - based decision - making and attentional bias to alcohol - seeking following devaluation. *Addiction*, 108(7): 1241-1249

81. Rosse R, Miller M, Hess A, Alim T, & Deutsch S. 1993. Measures of visual scanning as a predictor of cocaine cravings and urges. *Biological Psychiatry*, 33(7): 554-556

82. Salvucci DD, & Goldberg JH. 2000. *Identifying fixations and saccades in eye-tracking protocols.* Proceedings of the 2000 symposium on Eye Tracking Research & Applications, pp. 71-78

83. Sayette MA, Martin CS, Wertz JM, Perrott MA, & Peters AR. 2005. The effects of alcohol on cigarette craving in heavy smokers and tobacco chippers. *Psychology of Addictive Behaviors*, 19(3): 263-270

84. Schneider W, & Shiffrin RM. 1977. Controlled and automatic human information processing: 1. detection, search, and attention. *Psychological Review*, 84(1): 1-66

85. Schoenmakers T, Wiers RW, & Field M. 2008. Effects of a low dose of alcohol on cognitive biases and craving in heavy drinkers. *Psychopharmacology*, 197(1): 169-178

86. Schoenmakers T, Wiers RW, Jones BT, Bruce G, & Jansen ATM. 2007. Attentional re-training decreases attentional bias in heavy drinkers without generalization. *Addiction*, 102(3): 399-405

87. Schoenmakers T, de Bruin M, Lux I, Goertz A, Van Kerkhof D, & Wiers R. 2010. Clinical effectiveness of attentional bias modification training in abstinent alcoholic patients. *Drug and Alcohol Dependence*, 109: 30-36

88. See J, MacLeod C, & Bridle R. 2009. The reduction of vulnerability through the modification of attentional bias: A real world study using a home-based cognitive bias modification procedure. *Journal of Abnormal Psychology*, 118(1): 65 - 75

89. Shiffman S, Gwaltney CJ, Balabanis MH, Liu KS, Paty JA, Kassel JD, ... & Gnys M. 2002. Immediate antecedents of cigarette smoking: an analysis from ecological momentary assessment. *Journal of Abnormal Psychology*, 111(4): 531

90. Shiffman S, Paty JA, Gnys M, Kassel JA, & Hickcox M. 1996. First lapses to smoking: Within-participants analysis of real-time reports. *Journal of Consulting and Clinical Psychology*, 64: 366-379

91. Shiffman S, Paty JA, Gnys M, Kassel JD, & Elash C. 1995. Nicotine withdrawal in chippers and regular smokers: Subjective and cognitive effects. *Health Psychology*, 14: 301-301

92. Shiffman S, & Waters AJ. 2004. Negative affect and smoking lapses: A prospective analysis. *Journal of Clinical and Consulting Psychology*, 72(2): 192-201

93. Shiffman S, Stone AA, & Hufford MR. 2008. Ecological momentary assessment. *Annual Review Clinical Psychology*, 4: 1-32

94. Silagy C, Lancaster T, Stead L, Mant D, & Fowler G. 2004. Nicotine replacement therapy for smoking cessation (review). *Cochrane Database Syst Rev*, 3

95. Sofuoglu M, DeVito EE, Waters AJ, & Carroll KM. 2013. Cognitive enhancement as a treatment for drug addictions. *Neuropharmacology*, 64: 452-463

96. Sofuoglu M, Herman AI, Li Y, & Waters AJ. 2012. Galantamine attenuates some of the subjective effects of intravenous nicotine and improves performance on a Go No-Go task in abstinent cigarette smokers: a preliminary report. *Psychopharmacology*, 224(3): 413-420

97. SRNT Subcommittee on Biochemical Verification. 2002. Biochemical verification of tobacco use and cessation. *Nicotine and Tobacco Research*, 4: 149-159

98. Stacy AW. 1997. Memory activation and expectancy as pospective predictors of alcohol and marijuana use. *Journal of Abnormal Psychology*, 106: 61-73

99. Stacy AW, & Wiers RW. 2010. Implicit cognition and addiction: a tool for explaining paradoxical behavior. *Annual Review of Clinical Psychology*, 6: 551

100. Stone AA, & Shiffman S. 2002. Capturing momentary, self-report data: A proposal for reporting guidelines. *Annals of Behavioral Medicine*, 24(3): 236-243

101. Swanson J, Swanson E, & Greenwald A. 2001. Using the Implicit Association Test to investigate attitude-behaviour consistency for stigmatised behaviour. *Cognition & Emotion*, 15(2): 207-230

102. Thush C, Wiers R, Ames S, Grenard J, Sussman S, & Stacy A. 2008. Interactions between implicit and explicit cognition and working memory capacity in the prediction of alcohol use in at-risk adolescents. *Drug and Alcohol Dependence*, 94(1-3): 116-124

103. Tiffany ST. 1990. A cognitive model of drug urges and drug-use behavior: role of automatic and nonautomatic processes. *Psychological Review*, 97(2): 147

104. Tiffany ST. 1997. New perspectives on the measurement, manipulation and meaning of drug craving. *Human Psychopharmacology: Clinical and Experimental*, 12(2): S103-S113

105. Volkow N, & Fowler J. 2000. Addiction, a disease of compulsion and drive: Involvement of the orbitofrontal cortex. *Cerebral Cortex*, 10(3): 318-325

106. Volkow ND, Fowler JS, & Wang GJ. 2004. The addicted human brain viewed in the light of imaging studies: brain circuits and treatment strategies. *Neuropharmacology*, 47: 3-13

107. Waters AJ, Heishman SJ, Lerman C, & Pickworth W. 2007. Enhanced identification of smoking-related words during the attentional blink in smokers. *Addictive Behaviors*, 32(12): 3077-3082

108. Waters AJ, & Leventhal AM. 2006. *Clinical relevance of implicit cognition in addiction.* In Cognition and Addiction, Oxford University Press, Oxford, England: 249-278

109. Waters AJ, & Li Y. 2008. Evaluating the utility of administering a reaction time task in an ecological momentary assessment study. *Psychopharmacology*, 197(1): 25-35

110. Waters AJ, Marhe R, & Franken IH. 2012. Attentional bias to drug cues is elevated before and during temptations to use heroin and cocaine. *Psychopharmacology*, 219(3): 909-921

111. Waters AJ, Miller EK, & Li Y. 2010. Effect of extensive testing on the IAT effect assessed in an ecological momentary assessment study. *Psychological Reports*, 106: 31-43

112. Waters AJ, & Sayette MA. 2006. Implicit cognition and tobacco addiction. In *Handbook on Implicit Cognition and Addiction*, ed. AW Stacy & RW Wiers. Thousand Oaks, CA: Sage

113. Waters AJ, Shiffman S, Bradley BP, & Mogg K. 2003. Attentional shifts to smoking cues in smokers. *Addiction*, 98(10): 1409-1417

114. Waters AJ, Shiffman S, Sayette MA, Paty JA, Gwaltney CJ, & Balabanis MH. 2003b. Attentional bias predicts outcome in smoking cessation. *Health Psychology*, 22(4): 378-387

115. Waters AJ, Szeto EH, Wetter DW, Cinciripini PM, Robinson JD, & Li Y. 2013. Cognition and craving during smoking cessation: An ecological momentary assessment study. *Nicotine & Tobacco Research*. Epub ahead of print

116. Weafer J, & Fillmore MT. 2013. Acute alcohol effects on attentional bias in heavy and moderate drinkers. *Psychology of Addictive Behaviors*, 27(1): 32

117. Wegner DM, & Schneider DJ. 2003. The white bear story. *Psychological Inquiry*, 14(3-4): 326-329

118. Weickert TW, Mattay VS, Das S, Bigelow LB, Apud JA, Egan MF, ... & Goldberg TE. 2013. Dopaminergic therapy removal differentially effects learning in schizophrenia and Parkinson's disease. *Schizophrenia Research*, 149: 162-166

119. Weickert TW, Terrazas A, Bigelow LB, Malley JD, Hyde T, Egan MF, ... & Goldberg TE. 2002. Habit and skill learning in schizophrenia: evidence of normal striatal processing with abnormal cortical input. *Learning & Memory*, 9(6): 430-442

120. Wiers RW, Gladwin TE, Hofmann W, Salemink E, & Ridderinkhof KR. 2013. Cognitive bias modification and cognitive control training in addiction and related psychopathology: Mechanisms, clinical perspectives, and ways forward. *Clinical Psychological Science*, 1(2): 192-212

121. Wiers RW, & Stacy AW, eds. 2005. *Handbook of Implicit Cognition and Addiction*. Thousand Oaks, CA: Sage Publications

122. Wilkinson L. 1999. Statistical methods in psychology journals: guidelines and explanations. *American Psychologist*, 54(8): 594

123. Williams J, Wellman N, Geaney D, Feldon J, Cowen P, & Rawlins J. 1997. Haloperidol enhances latent inhibition in visual tasks in healthy people. *Psychopharmacology*, 133(3): 262-268